at initial diagnosis II/III/IV 21%/14%/64%; no. of metastatic sites 1/>1 46%/54%; most common metastatic site liver; prior adjuvant therapy 33% (Mayo 5-FU/LV). Pts received a median of 12 cycles (range 1–12) of capecitabine + irinotecan + bevacizumab; capecitabine + bevacizumab range: 0–26. All 28 pts are evaluable for safety and 26 for efficacy. The overall response rate is 69% (3 CR, 15 PR); 2 pts (8%) have stable disease and 6 have progressed. One pt has died. Median PFS and median OS have not yet been reached. The only grade 3 adverse events are diarrhoea (11%), hand–foot syndrome (7%), fatigue (4%), mucositis (4%), enteritis (4%) and ileus (4%); there is one report of grade 4 leukopenia. All other adverse events are mild-to-moderate.
Conclusions: The capecitabine + irinotecan + bevacizumab combination appears to be highly active and well tolerated as first-line treatment for MCRC, providing support for further evaluation of this combination.

3069 POSTER

Study of CPT-11, oxaliplatin, UFT triple therapy (SCOUT) in advanced colorectal cancer (ACRC): an effective and well-tolerated regimen

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Background: Treatment-related toxicity and poor performance status can prevent patients from receiving second-line therapy after failure of first-line treatment. We investigated the feasibility of triple-drug therapy with irinotecan, oxaliplatin, and UFT with leucovorin (LV) in a phase I/II open-label dose-finding trial in patients with ACRC. Of particular interest was whether patients could benefit further from chemotherapy after disease progression.
Methods: Eligible patients aged ⩾18 y had histologically confirmed advanced, inoperable, measurable metastatic disease, no prior chemotherapy other than adjuvant 5-fluorouracil (5-FU) ⩾6 mo previously, and adequate bone marrow, liver, and kidney function. In phase I, patients received irinotecan 180 mg/m^2 on d1, oxaliplatin 85–100 mg/m^2 on d15, and UFT 200–300 mg/m^2/d with LV 90 mg/d on d1–21 of a 28-d cycle. The maximum tolerated dose (MTD) was established at irinotecan 180 mg/m^2, oxaliplatin 100 mg/m^2, UFT 250 mg/m^2/d, and LV 90 mg/d. Patients were treated at the MTD in the phase II study.
Results: Patients (median age 62 [range 24–79] y, ⩾3 marker lesions in 32 patients, disease confined to liver in 12 patients) were recruited, 25 in phase I and 20 added in phase II for a total of 29 at the MTD. Treatment was highly effective, with a response rate of 66% (95% CI 49–80%) in 38 evaluable patients and clinical benefit in 89% (95% CI 75–97%). At a median follow-up of 10.3 mo, median time to progression was 8.5 mo (95% CI −7.6 to 10.4 mo) in 40 evaluable patients; median overall survival (ITT population n = 45) was 16.8 mo (95% CI −11.3 to 28.3 mo). Two patients underwent resection of liver metastases (1 R0, 1 R1). Grade 3 adverse events at the MTD included: diarrhea (n = 3; 10%); neurotoxicity (n = 1; 3%); lethargy (n = 1; 3%). One patient had grade 4 cardiac toxicity. No hand–foot syndrome (HFS) was seen. In 30 patients with confirmed radiologic progression, 21 (70%) had second-line therapy (Table).

Second-line regimen	N
SCOUT retreatment[a]	8
Irinotecan/cetuximab	3
Mitomycin C/capecitabine	4
Oxaliplatin/5-FU	2
Capecitabine	1
Phase I studies	3

[a]Up to four 6-mo cycles.

Conclusions: In the first-line treatment of patients with ACRC, UFT plus LV with alternating irinotecan and oxaliplatin gives a high response rate, with minimal alopecia and neurotoxicity and no HFS, thus permitting administration of repeated treatment courses and resection in suitable patients. The SCOUT regimen is an effective and convenient treatment for patients with ACRC.

3070 POSTER

Bevacizumab in patients with previously treated metastatic colorectal cancer: preliminary results of a phase II study (bevacolor)

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Background: The activity of bevacizumab(Avastin®) as part of second-line therapies in metastatic colorectal cancer (mCRC) is currently under investigation. The aim of this study was to determine the safety and efficacy of adding bevacizumab (BV) to common chemotherapy regimens used in second-line therapy in mCRC.
Methods: A multicentre phase II study was conducted in fifty-three patients with mCRC progressing after first-line oxaliplatin or irinotecan-based chemotherapies. They received bevacizumab (BV) 2.5 mg/kg/week, until disease progression, on day 1 of a chemotherapy regimen chosen by the investigator.
Results: Overall, 35 men and 18 women, performance status 0 to 2, median age 62 (33−80) years, were treated. Ten patients (19%) had liver metastases and 39 patients (74%) had more than one metastatic site. The first-line treatment previously administered to patients was Folfox (53%), Folfiri (22%), Xelox (20%) and other chemotherapies (5%). Second line treatments included Folfiri (57%), Folfox (26%), Irinotecan (15%), Xeliri (2%). Patients received a median of 8 cycles (2−13) of chemotherapy and BV and 43 (81%) received BV at the dose of 5 mg/kg every 2 weeks.
After a follow up of 6 months, best response was assessed: one (2%) patient had a complete response (CR), 16 (30%) had partial response (PR), 29 (55%) had stable disease (SD) and 5 (9%) progressed. The rate of disease control defined as CR +PR +SD was 87% [95% CI, 78%-96%] and objective response rate (CR +PR) was 32% [95% CI, 19%-46%].
A total of 51 (96%) patients had adverse events and thirty-two (60%) had Grade 3/4 CTC AE toxicities including neutropenia in 11 (21%) patients, diarrhea in 7 (13%) and asthenia in 5 (9%). Grade 3/4 targeted toxicities (known to occur with BV) were reported in 6 (11%) patients, they included hypertension in 3 (6%) patients and thromboembolism in 3 (6%). Three deaths occurred mainly due to disease progression, no toxic death was observed.
Conclusions: The administration of BV, associated to chemotherapy is acceptable as 2nd line treatment in patients with mCRC, achieving an objective response rate of 32%. The toxicity profile of Bevacizumab in combination with standard chemotherapies in mCRC was acceptable. More details including progression free survival and overall survival will be given at the congress.

3071 POSTER

Impact of intensity modulated radiation therapy (IMRT) on bone marrow tolerance during combined treatment with chemotherapy for patients with anal canal cancer

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Background: IMRT has been introduced as a mean to improve sparing of normal structures during radiation therapy. Present study is reporting the experience of a single institution with the use of IMRT and conformal external beam radiation combined with chemotherapy for patients with anal canal carcinoma.
Materials and Methods: From 2004–2007, fifty patients with T2−4 squamous cell anal canal carcinoma were treated to doses of 54−59.8 Gy in 30−33 fractions without interruption and concurrently with 2 cycles of chemotherapy during weeks 1 and 6 of radiation using 5-Fluorouracil (5-Fu, 1000 mg/m^2/day, 96 hours continuous infusion) and Mitomycin C (MMC, 10 mg/m^2, bolus on day 1). Radiation was delivered with IMRT in 18 patients and 3D-conformal radiation therapy (3D-CRT) in 32 patients. Dose of 30 Gy in 15 fractions were prescribed to elective iliac and inguinal nodes and 54−59.6 Gy to the tumor bed and involved nodes. A two-phase CT-based planning is done for both techniques. Pelvic bone marrow was defined as the region extending from the iliac crests to the ischial tuberosities. Hematological toxicity was assessed by weekly blood counts

and scoring using the common toxicity criteria version 3. Dose volume analysis was performed for pelvic bone marrow (PBM) receiving 5, 10, 15, 20, and 25 Gy. The Wilcoxon rank sum-test was used for comparison of median locations, and the Bonferroni correction was used for multiple comparisons.
Results: Patients treated with IMRT and 3D-CRT had respectively 33% (6/18) G3 and 15.6% (5/32) G3−5 hematological toxicity. There were 4 HIV positive patients in the 3D-CRT as compared 1 patient in the IMRT group and no difference in the median age (62−63 years) in two-treatment groups. Table 1 shows the comparative mean dose volumes to PBM for both techniques. A significant difference is observed at low dose levels (5 to 15 Gy).
Conclusions: IMRT provides better dose conformity at high dose level but also increases significantly the exposed PBM volume to low radiation doses. The observed enhanced bone marrow toxicity during pelvic IMRT and chemotherapy for patients with anal canal cancer suggests a chemo-sensitizing effect of PBM at low dose radiation levels.

Table 1. Pelvic bone marrow toxicity as a function of dose volume parameters for anal canal cancer patients treated with IMRT and CRT in combination with chemotherapy (BM+ is grade 3 or higher BM toxicity)

Technique	Parameter	Toxicity	V5 (%)	V10 (%)	V15 (%)	V20 (%)	V25 (%)
3D-RT	Average		32.23	26.18	22.48	17.97	12.72
IMRT	Average	BM +	64.92	54.80	42.44	28.00	16.10
	P value (bilateral)		0.008	0.008	0.008	0.095	1.000
3D-RT	Average		35.73	31.51	27.57	24.02	19.26
IMRT	Average	BM−	48.42	38.92	29.22	16.70	7.42
	P value (bilateral)		1.000	1.000	0.841	0.310	0.008
	VolumeRatio IMRT/3DCRT	BM +	2.01	2.09	1.89	1.56	1.27
		BM−	1.36	1.24	1.06	0.70	0.39

3072 POSTER

Quantitative intra-operative assessment of peritoneal carcinomatosis – a comparison of three prognostic tools

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Aims: To compare the efficacy of three quantitative intra-operative assessment tools of peritoneal carcinomatosis used to select patients for combined modality treatment of cytoreductive surgery and Hyperthermic Intra-PEritoneal Chemotherapy (HIPEC).
Methods: 92 procedures performed between 1999 and 2005 were prospectively scored using the Simplified Peritoneal Cancer Index (SPCI) and a 7 Region Count. Using the SPCI tool, operative notes and pathological reports patients were retrospectively scored using the Peritoneal Cancer Index (PCI). The predictive power of the three prognostic tools on completeness of cytoreduction and overall survival was evaluated by a logistic regression and a receiver operating characteristic (ROC) curve.
Results: After a median follow-up of 31 months, the median overall survival was 25.6 months. The overall survival decreased from 26.2 to 7.3 months, when cytoreduction was incomplete ($p = 0.001$, hazard ratio 3.9, 95% CI 1.7−8.8). In the univariate analysis, both an increased PCI and SPCI, as well as an increased number of regions were associated with a decrease in probability of complete cytoreduction ($p < 0.05$). With complete cytoreduction as outcome, the ROC area for the PCI, SPCI and 7 Region Count were 0.92, 0.94 and 0.90 respectively ($p = 0.14$). Using a cut-off value of 16 in the PCI system ($p = 0.03$), 13 in the SPCI system ($p = 0.04$) and 6 regions in the 7 Region Count ($p = 0.0002$) the overall survival decreased significantly when the cut-off was scored or exceeded.
Conclusion: The PCI and the SPCI scoring systems, as well as the 7 Region Count, are useful and equally effective prognostic tools for completeness of cytoreduction and associated survival after cytoreductive surgery and intra-operative HIPEC. The 7 Region Count is adequate and may be preferred due to its practical simplicity.

3073 POSTER

Optimisation of radiotherapy planning for rectal cancer: a comparison of supine CT and MRI defined target and normal tissue dose volume data

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Background: We have previously demonstrated that the volume of bowel receiving higher dose levels in the pelvic radiation field for rectal cancer is not significantly different in the prone or supine position. This planning study compares supine CT and MRI defined gross tumour volumes (GTV) and planned target volumes (PTV), and dose to organs at risk (OAR).
Materials and Methods: 20 patients undergoing preoperative chemo-radiotherapy (CRT) for rectal cancer had planning CT scans in the prone and supine positions. Patients then had a T2 MRI scan in the same supine position. MR datasets were imported into Pinnacle TPS version 7.4f and manually fused with CT datasets, using bony anatomy. GTVs were delineated for CT (GTVCT) and MR (GTVMR) plans. All GTVs were reviewed by a single radiologist (GB). PTV Phase I and II were defined (PTVCT, MR Phase I, II). The Phase II volume encompassed the entire portion of the rectum containing the tumour with a 2 cm margin in all dimensions. OARs (bladder, femoral heads, penile bulb, levators and bowel within and 2 cm superior to the PTV) were outlined.
All patients received CT-planned conformal RT, phase I pelvis: 45 Gy/25 fractions and phase II: 5−9 Gy/3−5 fractions. A 3 field conformal technique using multi-leaf collimation was employed for both phases. The volume of each OAR receiving doses in increments of 5 Gy to 50 Gy was calculated using Dose Volume Histograms (DVH) of composite phase I and II plans. P-values were obtained using a student t-test.
Results: For these first 5 patients analysed, GTVMR were consistently smaller than GTVCT (31.943 vs 38.877; 9.061 vs 7.092; 19.656 vs 35.284; 3.281 vs 16.36; 187.523 vs 277.833, all cm^3, $p = 0.21$). While PTVCT and PTVMR phase I volumes were similar, PTVMR phase II were significantly smaller than PTVCT volumes in all cases (565.88 vs 625.258; 270.104 vs 293.172; 364.378 vs 450.457; 464.169 vs 712.476; 1017.92 vs 1126.93, all cm^3, $p = 0.05$). Composite OAR DVHs are currently similar for all dose levels.
Conclusions: MRI planning results in a trend to smaller GTVs and significantly smaller phase II volumes, and may prove to reduce dose to OARs. Given the proven superiority of MRI over CT in staging and delineation of rectal tumours, it is assumed that these smaller MR volumes are more accurate. Final results will be presented at the meeting.

3074 POSTER

Pulmonary resection for metastases from colorectal cancer

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Background: The lung is the most common extra-abdominal site for metastases from colorectal cancer. Patients with untreated metastatic disease have a median survival of less than 10 months and a 5-year survival of less than 5%.
The purpose of this study was to evaluate long-term survival in patients who underwent pulmonary resection for metastases from colorectal cancer.
Methods: Between Jan 1990 and Jan 2005, 23 patients underwent 29 operations for resection of lung metastases.
Results: Median age was 68 years (range: 46−80 years). Median follow-up was 30 months (range:12–149 months). The two-year and five-year overall survival was 64% and 26% respectively. Of the 23 patients, 16 patients had a solitary lesion and 7 patients had multiple lesions. The five-year survival was 23% and 33%, respectively (NS).
The median disease free interval (DFI) – the interval between colon resection and the appearance of lung metastases – was 43 months (1–168). Ten patients had a DFI < 36 months and 13 patients had a DFI of more than 36 months. The three-year survival was 20% and 38%, respectively (NS).
Recurrence of lung metastases was diagnosed in 7 patients; 3 patients underwent a second resection. They are are alive today with a median follow-up of 18 months. Patients who did not undergo a second resection had a median survival of 12 months.