

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 chemosensitizing 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	BM +	32.23	26.18	22.48	17.97	12.72
	Average		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	BM–	35.73	31.51	27.57	24.02	19.26
	Average		48.42	38.92	29.22	16.70	7.42
	P value (bilateral)		1.000	1.000	0.841	0.310	0.008
IMRT	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

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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.

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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 chemoradiotherapy (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 analysed 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.

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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 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.

Conclusions: Pulmonary resection for metastases from colorectal cancer does produce longer survival, even in patients with multiple lesions and recurrent metastases.

Oral presentations (Thu, 27 Sep, 09.00–11.00)

Gastrointestinal malignancies – non colorectal cancer

3500

ORAL

Preliminary results from a phase II, randomized, double-blind study of sorafenib plus doxorubicin versus placebo plus doxorubicin in patients with advanced hepatocellular carcinoma

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Background: Sorafenib, a tyrosine kinase inhibitor with multiple targets, including Raf kinase and the vascular endothelial growth factor receptor (VEGFR), has demonstrated modest single agent activity in hepatocellular carcinoma (HCC) (Abou-Alfa et al: JCO 2006;24: 4293–4300). Here we report the findings of an unplanned interim analysis, requested by the external data safety monitoring board, of a phase II, randomized, double-blind study, conducted to assess sorafenib plus doxorubicin (dox) versus placebo plus dox in patients with advanced HCC.

Material and Methods: Patients with advanced HCC, ECOG Performance Status (PS) of 0–2, Child–Pugh A only and no prior systemic therapy, received dox 60 mg/m² i.v. every 21 days plus either sorafenib 400 mg orally twice daily or placebo, for a maximum of six cycles (18 weeks) of dox. Patients could continue on single-agent sorafenib or placebo beyond 18 weeks until disease progression. The primary efficacy endpoint was time to progression (TTP) by external review. Secondary endpoints included overall survival (OS), response rate according to RECIST criteria, and toxicity. Twenty-six progression events have occurred at this analysis.

Results: A total of 96 patients were randomized (sorafenib plus dox, n = 47; placebo plus dox, n = 49); 76% were male, 91% had an ECOG PS of 0–1, and the median patient age was 65 years. Baseline patient characteristics were balanced between treatment arms. Data are presented in the table. The TTP and OS of the placebo/dox control arm fall within the range of the historically reported data for dox alone.

Conclusions: In this preliminary analysis, TTP and OS in the sorafenib/dox arm appear to be encouraging, and toxicity appears tolerable. Per the external DSMB recommendation, the trial has been unblinded and remaining patients on the control arm have been crossed over to sorafenib. Updated analyses will be presented at the meeting.

	Time to progression	Overall survival	Response rate (CR+PR) %	Grade 3/4 fatigue	Grade 3/4 neutropenia
Sorafenib/dox	8.5 mo	14.0 mo	4.3	10.6%	36.2%
Placebo/dox	2.8 mo	5.6 mo	2.0	6.3%	41.7%

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ORAL

Capecitabine/cisplatin vs. continuous infusion of 5-FU/cisplatin as first-line therapy in patients (pts) with advanced gastric cancer (AGC): a randomised phase III trial

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Background: Capecitabine has proven efficacy and safety in a number of tumours, particularly colorectal, breast and gastric cancers. A phase II study in AGC suggested that capecitabine plus cisplatin (XP) has comparable efficacy to the standard 5-fluorouracil/cisplatin (FP) regimen, with potential safety and convenience advantages. We compared XP and FP as first-line treatment for AGC.

Materials and Methods: In this randomised, open-label, multicentre study, pts with previously untreated AGC received either oral capecitabine (1000 mg/m² bid days 1–14) plus cisplatin (80 mg/m² i.v. day 1) every 3 weeks (XP arm) or 5-FU (800 mg/m²/day continuous infusion, days 1–5) plus cisplatin (80 mg/m² i.v. day 1) every 3 weeks (FP arm). Pts were treated until disease progression or unacceptable toxicity. Primary endpoint: non-inferiority in progression-free survival (PFS), defined as upper limit for 95% CI of the hazard ratio (HR) of

Results: 316 pts were randomised. Median number of treatment cycles per arm was 5. Median follow-up was 21.2 months (range 13–34) for XP, and 21.0 (14–33) for FP. In the per protocol population, median PFS for XP was 5.6 months (95% CI 4.9–7.3) vs. 5.0 months for FP (95% CI 4.2–6.3). Primary endpoint was met with HR of 0.81 (95% CI 0.63–1.05, p < 0.001 vs. non-inferiority margin of 1.25); non-inferiority was highly significant. Median overall survival (OS) for XP was 10.7 months (95% CI 9.5–11.5) vs. 9.5 months for FP (95% CI 7.5–11.4). For OS, XP was significantly non-inferior vs. FP (HR = 0.89, 95% CI 0.68–1.17, p = 0.0146 vs. non-inferiority margin of 1.25 in per protocol population). XP was significantly superior to FP in terms of objective response rate (ORR, RECIST: 41% vs. 29%; p = 0.0295 in ITT population). Both treatments were well tolerated and had similar safety. Most common treatment-related grade 3/4 adverse events: neutropenia (occurring in 16% of XP vs. 19% of FP pts), vomiting (7% vs. 8%), stomatitis (2% vs. 6%), diarrhoea (5% vs. 5%), anaemia (3% vs. 2%). Rate of hand–foot syndrome was low (22% vs. 4%) relative to other studies. **Conclusions:** XP showed highly significant non-inferiority for PFS and OS vs. FP and had similar safety. XP was also significantly superior to FP in terms of ORR.

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ORAL

Final results of a randomized phase III trial in patients with advanced adenocarcinoma of the stomach receiving first-line chemotherapy with fluorouracil, leucovorin and oxaliplatin (FLO) versus fluorouracil, leucovorin and cisplatin (FLP)

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Background: Cisplatin-based chemotherapy is a standard option in advanced gastric cancer. However, treatment results have been unsatisfactory so far, with a progression-free survival (PFS) of 3 to 4 months and an overall survival (OS) of 6 to 9 months. In addition, treatment regimens are too intense and toxicity is considerable. The aim of this trial was to determine whether FLO prolongs PFS and reduces toxicity as compared to FLP.