(PC). After disease progression, there is no standard regimen available. In a previous phase II trial, S-1 has been reported to show marginal efficacy, achieving a response rate of 15%, a median progression-free survival (PFS) of 2.0 months and a median overall survival time (MST) of 4.5 months in Gem-refractory PC patients. The schedule of Gem administration, with fixed dose rate (FDR) infusion of 10 mg/m^2/min, would maximize the intracellular rate of accumulation for Gem triphosphate, and may improve clinical efficacy. The aim of this study was to determine the dose-limiting toxicity (DLT) and maximum-tolerated dose (MTD) of combination therapy with FDR-Gem and S-1 in patients with Gem-refractory PC.
Materials and Methods: Gem-refractory patients with histologically or cytologically proven metastatic PC were enrolled. The patients received Gem intravenously as an FDR (10 mg/m^2/min) on day 1 and S-1 orally twice daily from days 1 to 7. Cycles were repeated every 14 days until disease progression. Patients were scheduled to receive Gem (mg/m^2/week) and S-1 (mg/m^2/day) at four dose levels: 800/80 (level 1), 1,000/80 (level 2), 1,200/80 (level 3) and 1,200/100 (level 4).
Resuls: A total of 15 patients (pts) were enrolled in this study between June 2006 and April 2006. All three pts at the level 4 demonstrated DLT involving grade 4 neutropenia in two pts and grade 3 stomatitis in one. The MTD was Level 3. Fourteen pts are currently evaluable for response in this ongoing trial. There have been 4 confirmed partial responses (27%), 8 pts with stable disease, and only 2 pts with progressive disease. The median PFS was 3.5 months and MST has not been reached. Final results will be presented at the meeting.
Conclusions: This biweekly, outpatient regimen may offer a good compliance and quality of life, and may be a promising treatment for Gem-refractory PC patients. This regimen will be evaluated in Phase II studies on Gem-refractory PC patients.

3545 POSTER

Long-term results of the phase II study on radiotherapy combined with nedaplatin and 5-FU for postoperative locoregional recurrent esophageal cancer

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Background: Although the effectiveness of radiotherapy with concurrent administration of several anti-tumor drugs for postoperative recurrent esophageal cancer has been demonstrated, the results are not satisfactory. In June 2000, we started a phase II study on treatment of postoperative locoregional recurrent esophageal cancer with radiotherapy combined with nedaplatin and 5-fluorouracil. We have reported a preliminary result of the present study, however, we show the long-term results of the phase II study on this occasion.
Materials and Methods: From June 2000 to May 2005, 32 patients with locoregionally postoperative recurrent esophageal cancer were treated with radiotherapy (60 Gy/30 fractions/6 weeks) combined with chemotherapy consisting of two cycles of nedaplatin (70 mg/m^2/2 hours) and 5-fluorouracil (500 mg/m^2/24 hours for 5 days). The primary endpoint of the present study was overall survival rate, and the second endpoints were irradiated-field control rate, tumor response and toxicity. The mean follow-up period of survival patients was 41.6 months (range, 24.0 to 80.0 months).
Results: The 3-year and 5-year overall survival rates were 35.7% and 22.3%, respectively, with a median survival period of 22.5 months (95%C.I.= 12.8−32.2), and the 5-year local control rates were 71.4%. Complete response and partial response were observed in 18.8% and 53.1% of the patients, respectively. Grade 3 or higher leukocytopenia and thrombocytopenia were observed in 37.5% and 3.1% of the patients, respectively, but renal toxicity of grade 3 or higher was not observed. The regimen was completed in 84.4% of the patients.
In univariate analysis, the difference between survival rate in preradiotherapy performance status ($p = 0.031$), number of recurrent regions ($p = 0.018$) and recurrent pattern [worse for patients with anastomotic recurrence ($p = 0.036$)] were statistically significant.
Conclusions: Radiotherapy combined with nedaplatin and 5-FU is a safe and effective salvage treatment for postoperative locoregional recurrent esophageal cancer.

3546 POSTER

(XELOX)Capecitabine plus Oxaliplatin: clinical efficacy and safety in first-line treatment for metastatic gastric cancer

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Background: Capecitabina is a oral fluoropyrimidine with proven efficacy and favourable safety in colorectal cancer, whose administration does not require hospitalisation or placement of central iv line.
The trial was designed to evalute the efficacy of XELOX in metastatic gastric cancer.
Materials and Methods: To date 22 pts were enrolled in this study and treated with Oxaliplatin 120 mg/mq on day 1 and capecitabine 1.000 mg/mq twice daily from day 2 to day 15 every 3 weeks until disease progression or unaccepted toxicity. The evalutation of efficacy was performed every 3 cycles.
The characteristics of enrolled patients were: M/F = 13/9, Median age 56 yrs; median ECOG status 1 (range 0−2), all patients had adequate haematological, liver and renal function. The sites of disease were liver 10 pts, lymph nodes 7 pts, bone 1 pts and peritoneum 4 pts.
Results: All patients were evalutable for efficacy and toxicity. Were registered 3 RC and 6 RP with an overall Response Rate of 40%, in 8 pts we registreted a SD, 5 patients progressed. Two patients of 3 with RC had a single liver localization. The schedule was well tolerated, the main G 3/4 toxicity (according to NCI-CTC) observed were neutropenia 13% of the pts, diarrhoea 8% of pts. Neuropathy G2 was recorded in 3 pts (13%). No treatment related was reported.
Conclusions: XELOX appears to be effective and well tolerated in first-line and treatment of pts with metastatic gastric cancer. These results are superior to those of historical controls from this institution, but is necessary to confirm these data with a longer follow up and more patients.

3547 POSTER

Image-guided intensity modulated radiation therapy (IG-IMRT) for extrahepatic cholangiocarcinoma: Results from a mature case control comparison with conventional radiotherapy (CRT)

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Purpose: Cholangiocarcinomas are comparatively rare neoplasms, and the optimum role of radiotherapy remains to be determined. The specific aim of this study was to report the clinical results of a single-institution cholangiocarcinoma series treated with modern radiotherapeutic techniques, and to ascertain if clinical benefit was observed using ultrasound (US) image-guided intensity-modulated radiation therapy (IG-IMRT).
Methods and Materials: From 2001 to 2005, 11 patients with primary adenocarcinoma of the extrahepatic bile ducts were treated by daily US-guided IG-IMRT to a mean dose of 57 Gy. To compare outcomes, data from a sequential series of 8 patients treated between 1995 and 2005 with conventional radiotherapy techniques (CRT) were collected in a comparator set. Demographic and treatment parameters were collected. Endpoints included treatment-related acute toxicity and survival.
Results: A statistically significant higher mean dose was given to patients receiving IG-IMRT compared to CRT, 57 vs. 45 Gy ($p < 0.01$). At last contact 3 patients were living, with a median follow-up of 32 months or those alive at last contact. Median estimated survival for all 19 patients was 11.1 months (range 2−62 months). 1-and 3-year survival for the IG-IMRT cohort was 64% and 23%, compared to 12.5% and 0% for the CRT patients. A statistically significant survival differential between IG-IMRT and CRT cohorts was observed (median 15.0 vs 6.9 months, $p = 0.01$). Surgical resection was associated with improved survival ($p < 0.01$). One IG-IMRT patient (9%) experienced an RTOG acute toxicity score >2, specifically upper GI grade 3 nausea/vomiting requiring tube or parenteral support; no CRT patients experienced a score >2. The most commonly reported GI toxicity requiring medication (RTOG Grade $\geqslant 2$) was nausea and abdominal pain relieved with oral medication, experienced by 25% of CRT patients and 54% of IG-IMRT patients ($p =$ n.s.).
Conclusion: This hypothesis generating series presents the first mature clinical outcomes of extrahepatic cholangiocarcinomas treated with IG-IMRT. IG-IMRT shows potential for improved survival in biliary tract tumors,

and dose escalation using IG-IMRT represents a reasonable approach which should be further investigated in future prospective trials.

3548 POSTER

A phase II study of S-1 and irinotecan combination chemotherapy in patients with advanced gastric cancer as a first-line therapy

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Background: Irinotecan plus intravenous 5-FU with leucovorin is effective against gastrointestinal cancer. S-1 is an oral fluoropyrimidine derivative combining tegafur with the modulators 5-chloro-2,4-dihydropyrimidine and potassium oxonate. S-1 has a high response rate of about 40% in advanced gastric cancer (AGC). We evaluated antitumor activity and toxicities of S-1 and irinotecan combination in patients with AGC as a first-line therapy.
Methods: Patients with histologically confirmed AGC with unresectable or metastatic diseases, measurable lesions, PS 0−2, age between 18 and 70, and no contraindication to chemotherapy were eligible for this study. Treatment included S-1 40 mg/m^2 p.o. twice daily on days 1−14 and irinotecan 150 mg/m^2 i.v. on day 1 every 3 weeks until disease progression or unacceptable toxicities.
Results: Between Sep 2005 and Mar 2007, total 45 patients (pts) were enrolled and 41 pts were analyzed because 4 pts were too early for analysis. The median age was 56 years (range, 36−70). After a median 6 (range, 1−20; total, 291) cycles of chemotherapy, 38 pts were evaluable for response and 40 pts (290 cycles) for toxicity. In intention-to-treat analysis, the overall response rate was 48.8% (95% C.I., 33.5%-64.1%), including 0 CR, 20 PRs. After a median follow-up of 8.1 months (range, 1.1−18.6), median time to progression was 5.7 months (95% C.I., 4.5−6.8) and median overall survival was 9.3 months (95% C.I., 5.0−13.6). Commonly observed grade 3/4 adverse events were neutropenia (30.0% of pts), vomiting (12.5%), nausea (10.0%) and diarrhea (7.5%). Treatment was delayed during 9 cycles (3%). The dose of S-1 and irinotecan were reduced during 71 cycles (24.5%) and 69 cycles (23.8%), respectively. There were two pts of neutropenic fever, but none of treatment-related death.
Conclusion: S-1 and irinotecan combination chemotherapy was active and tolerable as a first-line therapy for AGC.

3549 POSTER

Venous thromboembolism as a complication of chemotherapy for upper gastrointestinal malignancy

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Background: Patients with metastatic malignancy are at an increased risk of venous thromboembolism (VTE) both by the nature of their disease and the treatment they receive, particularly with cisplatin based chemotherapy. While previously diagnosed at presentation with symptoms, modern multi-slice CT has led to the diagnosis of increasing numbers of asymptomatic thromboembolic events.
Patients in the UK with operable oesophagogastric cancer are commonly treated with peri-operative cisplatin containing chemotherapy, with cisplatin carrying a particular risk of VTE. In our practice we have seen increasing numbers of patients with early stage disease diagnosed with asymptomatic VTE. VTE carries a significant morbidity both in terms of the disease itself and associated treatment, and in early disease may impact on the safety of subsequent surgery.
Methods: We reviewed the case notes of all patients referred to our centre over a 12 month period for management of oesophageal, gastric or oesophagogastric junction cancers.
Results: 108 patients were referred to our centre from 01/01/05 to 31/12/05 for management of an upper gastrointestinal malignancy. 61 patients received systemic chemotherapy, 43 for local disease (70.5%) and 18 for metastatic disease (29.5%). 53 (86.9%) of the patients receiving chemotherapy were treated with a cisplatin containing regimen. There were 11 cases of VTE; 5 were of pulmonary embolus, all diagnosed on staging scans, 1 at the time of diagnosis and four at post chemotherapy assessment. The remaining 5 were lower limb deep vein thrombosis (DVT) and 1 upper limb catheter associated DVT. Of those patients receiving cisplatin chemotherapy 9 had a diagnosis of VTE (17.0%; 95% CI 8.1−29.8%). Within the overall chemotherapy group 10 patients had an episode of VTE (16.4%). The Odds Ratio for an episode of VTE in patients undergoing chemotherapy was 9.0 (95% CI 1.4−56.2, p = 0.015). 31 of the 61 patients receiving chemotherapy were planned for subsequent surgery. 5 of those developed an episode of VTE (16.1%), 1 requiring placement of an IVC filter prior to surgery.
Conclusions: VTE is a significant problem in this population, particularly those receiving cisplatin-containing chemotherapy. Our data shows similar rates of VTE in an unselected population to that reported in the REAL 2 trial (18% and 15% in the cisplatin containing arms). We propose a prospective study of the role of thromboprophylaxis in this patient group.

3550 POSTER

Capecitabine plus hepatic intra-arterial epirubicin and cisplatin in unresectable biliary cancer: a phase II study

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Background: the prognosis of advanced biliary tract cancer is very poor. The rationale for the use of intra-arterial hepatic chemotherapy is related to the natural history of these tumors, with a growth through a local extension rather than distant metastases and to the high hepatic extraction upon the first pass of some drugs that reach bile canaliculi at high concentration. Aim of this study is to evaluate the activity of hepatic intra-arterial infusion of epirubicin and cisplatin combined with oral capecitabine, in patients (pts) with unresectable biliary cancers.
Materials and Methods: twenty pts were treated by bolus infusion of epirubicin 50 mg/m^2 and cisplatin 60 mg/m^2 in the hepatic artery through an angiografic catheter placed with Seldinger technique on day 1, combined with oral capecitabine 1000 mg/m^2 bid, from day 2 to day 15.
Results: tumor site were intrahepatic bile ducts in 12 patients, gallbladder in 7 and choledochus in 1. Nineteen pts are evaluable for response. Partial responses were observed in 6 pts (31.5%), stable disease in 9 (47.5%), progression in 4 (21%). The median progression-free and overall survival periods were 11.6 and 18.0 months, respectively, and 1-year survival was 74%. One patient died after the first cycle because of G4 gastro-intestinal toxicity. The other pts had a good tolerance, with minimal hematologic toxicity and only 1 G3 vomiting.
Conclusions: this combined intra-arterial and oral approach to pts with biliary carcinomas was found to be active and safe and seems to produce interesting survival.

3551 POSTER

Role of adjuvant chemoradiotherapy for ampulla of Vater cancer

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Background: The purpose of this study is to evaluate the role of adjuvant chemoradiotherapy for ampulla of Vater cancer.
Materials and Methods: Between January 1991 and December 2002, 118 patients with ampulla of Vater cancer underwent en bloc resection. There were 69 males and 49 females, and median age was 57 years (range; 28−78). Forty patients had Whipple's operation, and 78 had pylorus-preserving pancreaticoduodenectomy. Forty-one patients received adjuvant chemoradiotherapy [CRT(+) group], and 77 did not [CRT(−) group]. Postoperative radiotherapy was delivered to tumor bed and regional lymph nodes up to 40 Gy at 2 Gy per fraction with a two-week planned rest. Intravenous 5-fluorouracil (500 mg/m^2/day) was given on day 1 to 3 of each split course. The median follow-up period was 65 months.
Results: Despite more advanced pathologic features of T stage, N stage and histologic differentiation in CRT(+) group (p = 0.0012, 0.0013, and 0.0472, respectively), the 5-year overall survival rates of CRT(−) and CRT(+) groups were comparable (66.9% and 52.8%, respectively, p = 0.4397). The 5-year local-regional relapse-free survival rates of CRT(−) and CRT(+) groups were 79.9% and 80.2%, respectively (p = 0.9306). When age, type of operation, T stage, N stage, histologic differentiation, and the use of adjuvant chemoradiotherapy were incorporated into