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

Cox proportional hazard model, there were an improvement of local-regional relapse-free survival (p = 0.0050), and a trend of better overall survival (p = 0.0762) with the use of adjuvant chemoradiotherapy. In a subgroup analysis on patients with nodal involvement (n = 38), the use of chemoradiotherapy was correlated with increased overall and local-regional relapse-free survival on multivariate analysis (p = 0.0235 and 0.0095, respectively). The benefit of adjuvant chemoradiotherapy was significant for local-regional relapse-free survival (p = 0.0319), but not for overall survival (p = 0.4544) in patients with T3/T4 disease (n = 40).
Conclusions: Adjuvant chemoradiotherapy enhances locoregional control, and possibly overall survival in patients with ampulla of Vater cancer after curative resection.

3552 POSTER

Impact of the body mass index on the outcome of patients with cancer of the esophagogastric junction after surgical resection

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According to the classification of Siewert, cancer of the gastroesophageal junction is subdivided into Type I, II, or III dependent on its localization. Type I cancers are considered to be distal esophageal cancers, which are treated with esophageal resection. Type II and III cancers are considered to be gastric cancers and are treated with extended gastrectomy including resection of the distal esophagus. We were interested to evaluate the impact of body mass index (BMI) on postoperative complications, length of stay in the ICU, total hospital stay, and overall survival.
From 2000 to 2006, 108 patients with cancer of the esophagogastric junction were operated in our department. We divided the patients into two groups according to BMI. Fifty-six patients (52%) presented with a BMI below 25 kg/m2 (group 1) and fifty-two patients (48%) above 25 kg/m2 (group 2). Type I cancers (n = 26; 24%) were equally distributed between groups 1 and 2 with 13 patients in each group. Type II cancers (n = 61; 56%) were the most frequent types and occurred more often in group 2 (34 vs 27), and Type III cancers (n = 21; 19%), had a higher prevalence in group 1 (16 vs 5).
Pulmonary complications were observed in 33 patients (respiratory in sufficiency n = 12, pneumonia n = 12, bronchitis n = 7, lung embolism n = 2). There was no statistically significant difference between groups 1 and 2. However, both lung embolisms were seen in group 2. Eighteen patients developed surgical complications (anastomotic leakage n = 7, chylus fistula n = 1, intraabdominal abscess n = 3, intrapleural abscess n = 2, abscess of the abdominal wall n = 3, and bleeding n = 2). There was also no statistically significant difference between groups 1 and 2. Functional complications occurred in 29 patients (dysphagia n = 5, nausea n = 5, heart burn n = 4, impaired enteral nutrition n = 6, vomiting n = 9). We found no statistically significant difference between groups 1 and 2. However, impaired enteral nutrition and vomiting was observed more frequent in group 2. The median time in the ICU was 3 days in group 1, and 5 days in group 2 (p = 0.021). The median hospitalization time was 14 days in both groups. Overall survival after a follow up of 42 months was 34% in group 2 and 25% in group 1 (p = 0.961). Recurrence free survival was 48% in group 1 and 42% in group 2 (p = 0.596).
Our data show that surgery for cancer of the cardia can be performed independent of the BMI.

3553 POSTER

Phase I/II study of S-1 in patients (pts) with advanced hepatocellular carcinoma (HCC): Results of phase I part – Correlation between pharmacokinetics (PK) and hepatic dysfunction

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Background: S-1 is an oral formulation combining tegafur (FT), gimeracil (CDHP), and oteracil potassium (Oxo). The standard dose is 80 mg/m^2 bid for gastrointestinal, head and neck, breast, and lung cancers in Japan. The liver plays an important role in the conversion of FT to 5-FU, as well as the degradation of 5-FU. S-1 is expected to be effective against HCC, but nearly all pts with HCC have hepatic dysfunction. This study was designed to examine the correlation between the PK of S-1 and hepatic dysfunction and to determine the recommended dose of S-1 for pts with advanced HCC. In addition, we compared PK parameters in pts with HCC with those in patients with pancreatic cancer (PC) and biliary tract cancer (BTC).
Materials and Methods: Eligibility criteria were advanced HCC, unresectable/incurable by ablation or TACE, pathological and/or clinical confirmation of the diagnosis, at least one measurable lesion, an ECOG performance status (PS) of 0 to 2, Child-Pugh class A or B, adequate organ functions, and written consent. The starting dose of S-1 (level 1) was about 64 mg/m^2 bid (80% of standard dose) on days 1−28 of a 42-day cycle. Level 2 was 80 mg/m^2. A standard 3+3-design and standard definitions of DLT were employed. PK analyses were performed to determine the plasma concentrations of the S-1 components (FT, CDHP, and Oxo) and 5-FU on days 1 and 8. The PK parameters were compared with those in 8 pts with PC and 8 pts with BTC who were enrolled in each phase II trial.
Results: Nine pts with HCC (level 1: 3 pts, level 2: 6 pts), including 3 with Child-Pugh class B were enrolled. All pts had a PS of 0. The most common toxicities were thrombocytopenia, leukopenia, neutropenia, and anorexia. > Grade 3 toxicity was rare. There was no DLT at level 1. At level 2, DLT occurred in 2 pts with Child-Pugh class B. One had grade 3 anorexia, and the other had grade 2 rash, requiring more than 8 consecutive days of rest. There were no significant differences in PK parameters among pts with Child-Pugh class A, B, and the 16 pts with PC and BTC. Two pts (level 1: 1 pt, level 2: 1 pt) had a partial response, giving an overall response rate of 22% (2/9).
Conclusions: Hepatic dysfunction (Child-Pugh class A or B) did not significantly affect the PK parameters of S-1 or its metabolites. Although S-1 should be carefully given to pts with Child-Pugh class B, S-1 at 80 mg/m^2 bid is tolerated in pts with advanced HCC. This dose is recommended for the phase II part of this study.

3554 POSTER

Phase II study of oxaliplatin with low dose leucovorin and bolus and continuous infusion 5-fluorouracil (Modified FOLFOX-4) for gastric cancer patients with malignant ascites

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Background: The clinical study about chemotherapy of gastric cancer patients with malignant ascites had limited because peritoneal seeding is not defined measurable lesion and generally patients had poor performance status. We evaluate the efficacy and toxicity of fortnightly modified FOLFOX-4 regimen in patients with peritoneal disseminated gastric cancer.
Methods: Gastric cancer patients who had cytologically confirmed malignant ascites were treated with cycles of oxaliplatin 85 mg/m^2 on day 1 plus leucovorin 20 mg/m^2, followed by 5-FU a 400 mg/m^2 bolus and a 22 hour continuous infusion of 600 mg/m^2 5-FU on days 1−2 every 2 week intervals.
Results: Forty-eight patients were enrolled in this study. Male to female ratio was 2:1. Median age was 47 (31−76). 22 patients (45.8%) were treated with modified FOLFOX-4 as a 1st line palliative treatment. 21 patients (43.8%) had ECOG performance status 2. 36 patients were assessable with measurable lesion. Twelve of the 36 patients demonstrated partial responses (PR). Ascties amount decreasing or disappearance was observed 17 (35.4%) patients. The median time to progression and overall survival time were 3.5 months (95% CI: 2.9−4.1 months) and 8.4 months (95% CI: 4.9−11.9 months), respectively. Totally 233 cycles of chemotherapy were done. Major hematologic toxicities included grade 1−2 anemia (53.9%), neutropenia (41.6%) and grade 3−4 neutropenia (15.8%). Six cycles were associated with neutropenic fever. The most common non-hematological toxicities were grade 2 and 3 nausea/vomiting (17%). There was no treatment related death.
Conclusion: Even though gastric cancer patient with malignant ascites accompanied poor performance status, modified FOLFOX-4 regimen was found to be a safe and effective.

3555 POSTER

The efficacy of early ^{18}F-fluorodeoxyglucose positron emission tomography following completion of definitive chemoradiotherapy in patients with esophageal carcinoma

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Background: To assess the value of early ^{18}F-fluorodeoxyglucose positron emission tomography (FDG-PET) scans following definitive chemoradiotherapy (CRT) in predicting clinical local response (CLR) or local relapse-free survival (LRFS) of esophageal cancer patients.
Methods and Materials: We retrospectively analyzed 25 esophageal cancer patients who were treated with curative CRT between January 2005 and December 2006. Median age of patients was 60 years (range,