calculated according to the Kaplan-Meier method, and the log-rank test was used to determine statistical differences between life tables, considering significant values of $p < 0.05$.

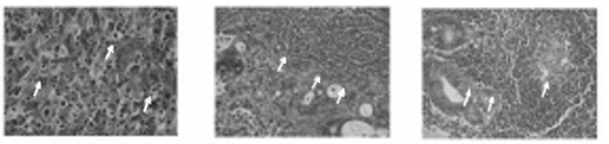

Fig. 1.

Results: Tumour associated mononuclear inflammatory cell, such as lymphocytes communicate with each other by extra cellular signals such as cytokines and their soluble receptors. Several cancer cell lines suggest that they are produced largely by tumour cell.
No statistically significant difference was observed in terms of age, sex, site of tumour, diameter, grading, CEA and Ca 19.9 levels, lymphatic and vascular invasion, classification (Lauren, Borrmann WHO).
The presence of IEL, PTL and CRL was showed in 26 patients (48.8%), 31 patients (56.8%) and 24 patients (43.2%) respectively.
Presence of IEL and CRL strong predicts a better disease free survival as shown in Figure 2. Patients with high levels of IEL and CRL demonstrate a lower rate of relapse ($p = 0.0003$ and $p = 0.005$ respectively). We did not found PLT and CRL in patients with relapse.

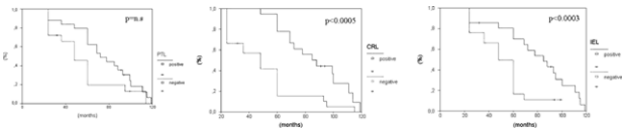

Fig. 2. Disease Free Survival

Conclusions: At present, there is no reason to expect a single predictive molecular factor to emerge that determines with high sensitivity and specificity that a patient is to expect disease recurrence or will profit from adjuvant therapy, respectively. But this preliminary study suggests that TILs may be useful as predictors of patient survival in surgically treated early stage gastric cancer.

767 POSTER

Targeting the tyrosine kinase platelet-derived growth factor beta-receptor (PDGFR-b) in advanced gastrointestinal malignancies-a phase I dose escalation study with imatinib in combination with 5-fluorouracil (5-FU) based chemotherapy

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Introduction: PDGFR-b is a mediator of tumor hypertension. Lowering of tumor interstitial hypertension has been shown to enhance tumor uptake of anticancer drugs. Imatinib, a specific inhibitor of the c-Kit, bcr-abl, and PDGFR gene products, enhanced the activity of 5-FU in animal models. This study was conducted to evaluate the feasibility, safety and efficacy of imatinib in combination with two different 5-FU based chemotherapeutic regimens in patients (pts) with advanced gastrointestinal malignancies.
Patients and methods: Pts were treated using a traditional 3-pts cohort dos-escalation strategy for defining the maximum tolerated dose (MTD) of imatinib in combination with chemotherapy, starting with 300 mg imatinib per day from day –4 to day 4 of chemotherapy with intravenous doses of 5-FU 2600 mg/m^2, leucovorin 200 mg/m^2 and oxaliplatin 85 mg/m^2 on day 1, qd15 (FLO, a modified FOLFOX-regimen) for 6 weeks (for gastric and colorectal cancer), or with 5-FU 2000 mg/m^2 and leucovorin 200 mg/m^2 on day 1 and 2, qd15 (FL) for 6 weeks (for pancreatic, cholangiocellular and gallbladder cancer). Prior to treatment, PDGFR-b and AKT in tumor and stroma were detected by immunohistochemistry. Imatinib pharmacokinetic assessments will be performed in pts receiving a dose of >500 mg/d or at the MTD.
Results: To date, 16 pts with previously treated gastrointestinal tumors were enrolled: 8 pts with pancreatic cancer, 5 pts with cholangiocellular cancer or cancer of biliary duct, 2 pts with colorectal cancer and 1 pt with gastric cancer. 6 pts were treated in the 300 mg cohort, 3 pts in the 400 mg cohort and 7 pts in the 500 mg cohort. All pts were evaluable for safety and 10/16 pts for efficacy. The treatment was generally well tolerated. NCI-CTC grade 3–4 toxicities were neutropenia (1/16), thrombocytopenia (1/16) and cardiac toxicity (1/16). Main grade 1–2 toxicities were anemia (9/16), neutropenia (5/16), nausea (5/16), constipation (5/16), and elevation of serum creatinine (5/16). Dose limiting toxicity occurred in 2 pt (NCI-CTC grade 4 neutropenia, mucositis, and infection in 1 pt in the 500 mg group, and grade 4 cardiac toxicity in the 300 mg group). 1 partial remission and 4 stable diseases of 10 evaluable pts were observed. The MTD has not been reached yet. Correlations to PDGFR-b expression and updated data will be presented at the meeting.
Conclusions: The combination of imatinib with oxaliplatin, 5-FU and leucovorin or 5-FU and leucovorin is feasible and safe.

Publication
GI – non-colorectal cancer

768 PUBLICATION

Oxaloplatin with biweekly, low dose leucovorin and bolus and continuous infusion 5-fluorouracil (modified FOLFOX 4) as salvage therapy for patients with advanced gastric cancer

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Background: To determine the activity and toxicities of low dose leucovorin (LV) plus fluorouracil (5-FU) regimen combined with oxaliplatin every two weeks (modified FOLFOX 4), as salvage therapy for patients with advanced gastric cancer.
Methods: Between December 2003 and December 2004, thirty-three patients were enrolled in this study. Patients were treated with oxaliplatin 85 mg/m^2 as a 2-hour infusion at days 1 plus LV 20 mg/m^2 over 10 minutes, followed by 5-FU bolus 400 mg/m^2 and 22 hour continuous infusion of 600 mg/m^2 at day 1–2. Treatment was repeated in 2 week intervals.
Results: The median age was 50 years (range: 31–74), 82% had a performance status of 0 or 1. Among 30 patients evaluable for tumor response, 8 patients achieved partial response, with an overall response rate of 26.7% (95% confidence interval (CI): 20.5–32.7%). Fifteen patients (50%) showed stable disease and seven patients (23.3%) progressed during the course of the treatment. The median time to progression was 3.5 months (95% CI: 2.6–4.4 months) and the median overall survival time was 7.9 months (95% CI: 5.9–9.9 months) from the start of the chemotherapy. Total 178 cycles analyzed for toxicity. Major grade 3/4 hematologic toxicities included neutropenia (48.4%) and thrombocytopenia (3.2%). There were only 2 cycles of neutropenic fever. The most common non-hematologic toxicities were grade 1–2 nausea/ vomiting (19.4%), diarrhea (12.9%) and neuropathy (12.9%). There was no treatment related deaths.
Conclusion: The modified FOLFOX 4 regimen is safe and effective regimen as salvage therapy in advanced gastric cancer patients.

769 PUBLICATION

Activity and tolerability of combination: capecitabine(c) plus gemcitabine(g) as first-line treatment in patients(pts) with locally advanced/metastatic pancreatic cancer

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The aim: of this study was to evaluate the efficacy and safety of C + G as first-line treatment in pts with locally advanced/metastatic pancreatic cancer.
Method: Eligible pts had measurable pancreatic cancer KPS $\geqslant$70% and adequate bone marrow, renal and hepatic function. Prior chemotherapy for pancreatic cancer and prior radiotherapy to the target lesion being measured in the study were not allowed. Pts received C 850 mg/m^2 orally twice daily on days 1–21 + G 1000 mg/m^2 by 30-infusion on days 1.8 and 15, every 4 weeks up to 6 cycles.
Results: Baseline characteristics of the 35 pts enrolled between march 2001 and February 2005: male/female (57% / 43%); mean age 57.5 + 8.2 years, liver metastases(49%). 32 pts are currently evaluable for safety and 30 for efficacy. The overall disease rate, 1-year progression-free survival and 1-year survival were 59% (9PR + 22SD), 57% and 58% respectively. Non-hematological adverse events (grade 2/3/4) were: vomiting (7/3/0%), nausea (8/3/0), anorexia (3/2/0%), hand–foot syndrome (6/0/0%), constipation (5/2/0%), general weakness (2/0/0%), insomnia (1/0/0%), and diarrhea (3/0/0%). Grade * neutropenia and grade3 thrombocytopenia occurred in 28% and 26% of pts, respectively.

Conclusion: The combination of C + G appears to be active and well tolerated as first-line treatment in pts with advanced/metastatic pancreatic cancer.

770 PUBLICATION

A phase II study of S-1 in patients with metastatic pancreatic cancer

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Background: The purpose of this study was to evaluate the efficacy and toxicity of S-1 in patients with metastatic pancreatic cancer. S-1, an oral anticancer agent, contains tegafur, gimeracil (CDHP: a dihydropyrimidine dehydrogenase inhibitor), and potassium oxonate (Oxo: an orotate phosphoribosyl transferase inhibitor) at a molar ratio of FT:CDHP:Oxo = 1:0.4:1.
Methods: Patients with histological or cytological diagnosis of measurable metastatic pancreatic adenocarcinoma not amenable to surgery or radiotherapy were eligible for the study. Other eligibility criteria included a Karnofsky performance status of 80 to 100%; an age of 20 to 74 years; adequate haematological, renal and liver functions; no prior chemotherapy; and written informed consent. S-1 was administered orally at 40 mg/sm twice daily for 28 consecutive days and then 14 days rest period as one course. Administration was repeated until the appearance of disease progression or unacceptable toxicity.
Results: Forty-one patients from seven institutions were enrolled. One patient deteriorated before receiving treatment and was excluded. Out of the 40 eligible patients, 15 patients had partial responses, for an objective response rate of 37.5% with a 95% confidence interval of 22.7–54.2%. And 11 patients had no change, 13 had progressive diseases, and one patient was not evaluated. The median survival time was 8.8 months (95% c.i.: 7.5–10.8 months). A clinical benefit response was achieved in four of the ten evaluable patients. The major drug-related toxicities were gastrointestinal toxicities such as anorexia (12.5%), diarrhoea (7.5%), nausea (7.5%), neutropenia (7.5%), though most of them were manageable. There was no drug-related death.
Conclusions: S-1 is effective and well tolerable as a single agent chemotherapy in patients with metastatic pancreatic cancer.

771 PUBLICATION

Combination of gemcitabine & cisplatin chemotherapy in unresectables gall bladder cancer

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Background: Adenocarcinoma of the gall bladder accounts for approximately 4% of all malignant neoplasm of the gastro-intestinal tract. Though surgical resection is the treatment of choice, majority of the cases are unresectable. Different chemotherapeutic agents including 5Flurouracil, Mytomycin C, Cisplatin, Methotrexate, Etoposide and Doxurobicin have been tried single or in combination. Partial response lasting from weeks to several months have been observed only in about 10%-20% of the cases and the median survival for patients with gall bladder cancer is approximately at around 4 months. Gemcitabine is a pyrimydine analogue of Deoxycytidine and has shown strong anti tumour activity in a variety of solid tumours. Cisplatin has synergistic activity with Gemcitabine. The aim of our study was to see the response rate of Gemcitabine and Cisplatin combination in unresectable gall bladder cancer and to see the tolerability in Indian-Asian pollution.
Materials and Methods: During period from November 2002 to December 2004 we selected consecutive 48 gall bladder cancers. All patients has histologicaly proven unresectable measurable gall bladder cancer. The inclusion criteria were performance status more than 60% (Kornofsky), no prior radiotherapy and normal liver (bilirubin <2) and kidney function (creatinine <2). All patient received Gemcitabine (1000 mg/m^2 intravenously over 30 minute) on day 1 and day 8 and Cisplatin (100 mg/m^2 divided D1 to D3) every 21 days. Response assessment was done by CT Scan after 3 cycles of chemotherapy. All 48 patients are eligible for efficacy and toxicity analysis.
Result: There were 9 (18.75%) complete responders, 15 (31.25%) partial responders, 13 (27.08%) with stable disease and 11 (22.91%) shows disease progression. The median time to progression was 20 weeks with range of 12–26 weeks. The median duration of response was 15 weeks (range 5.5–60 weeks). The median over all survival was 22 weeks (range 11–27 weeks) with 1year survival rate of 20.4%. WHO grade III or IV anaemia was seen in 8 & 5 patients respectively. Ten patients each experienced grade III or IV neutropenia while grade III or IV thompocytopenia was seen in 5 & 3 patients respectively.
Conclusion: The present study shows the Gemcitabin & Cisplatine combination was very useful in advanced unresectable gall bladder cancer. It was well tolerated by the the patients.

772 PUBLICATION

Treatment of advanced gallbladder cancer with gemcitabine (gem) or gemcitabine-cisplatin (gem-cispl)

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Gallbladder carcinomas (GBC) are often diagnosed at an advanced/metastatic stage amenable only to palliative surgery but in this case median survival is only around 8 to 12 weeks. Results of chemotherapy for advanced GBC are extremely poor with traditional treatment based on 5-FU.
Since 1997 we have been studying the effect of Gem. We retrospectively reviewed data of two different protocol treatments, we made possible. In both trials pts had similar characteristics, they all pts had measurable locally or metastatic GBC with histological or cytological proof, no prior chemotherapy nor radiotherapy. The main endpoint was RR and secondary endpoints were treatment toxicity and overall survival. We retrospectively review pts data and outcomes.
In first trial 26 pts were treated with Gem 1000 mg/m^2 i.v. for 30 minutes weekly for 3 weeks out of every 4 until disease progression and/or toxicity. In second cohort, 44 pts received Gem 1200 mg/m^2 and Cis 35 mg/m^2 on d1 and 8, every 21d for a total of 6 courses. Treatment was discontinued in case of unacceptable toxicity or disease progression. RR was evaluated by abdominal CT scan. Pts were treated on an outpatient basis.
Result: A total of 108 and 204 chemotherapy courses were given, 27% of pts for Gem alone and 63% of pts for Gem-cispl received at least 6 courses and 27% and 25% respectively received <2 courses. Twenty-five pts and 42 pts received at least one complete course of chemotherapy and were, therefore, evaluated for response. For Gem monotherapy the RR, CR and PR were 35/0/35% respectively, and for Gem-cisplt were 45/9/36%. All 26 and 44 pts were evaluated for toxicity. Four and 1 died due to disease progression, one pt died due to renal toxicity in the arm Gem-cispl. In one pt occurred hepatotoxicity grade 4 in arm gem alone. The main grade 3 hematology toxicities included thrombocytopenia (0% vs 2%), neutropenia (3.8% vs 23%) and anemia (3.8% vs 14%) in the group gem vs Gem-cispl respectively. Median survival time was 8.7 mos vs 7 mos for the entire population, 14.1 mos vs 9 mos for responders, and 6.1 mos vs 5 mos for non-responders.
Conclusion: Gem is active against advanced, unresectable recurrent and/or metastatic GC with a good tolerability. The low toxicity profile of Gem should be considered when a treatment choice is to be made for a patient with advanced GBC. Gem-cispl look like more active but survival was similar. A possible explanation may be that the treatment duration that was only six cycles in case of Gem-cispl.

773 PUBLICATION

Phase I study of docetaxel, cisplatin and 5-fluorouracil(TPF) as first-line chemotherapy in patients with advanced esophageal cancer. –Hokkaido Gastrointestinal Cancer Study Group (HGCSG) study-

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Background: This study was conducted to determine the maximum-tolerated dose (MTD), dose-limiting toxicity (DLT), and efficacy of a combination chemotherapy using docetaxel, cisplatin and 5-fluarouracil (TPF) in patients with advanced esophageal cancer.
Methods: Patients with previously untreated measurable metastatic esophageal cancer were included in this trial. Patients received this combination chemotherapy repeated every 28 days until progression