disease. Starting dose (dose level 1) were docetaxel 50 mg/m^2 on day 1, fixed dose intravenously cisplatin (15 mg/m^2/day) and continuous infusion 5-FU (800 mg/m^2/day) on day 1–4. Nine patients received this combination chemotherapy (TPF) at the two different dose level. DLT was defined as follows (according to NCI-CTC version 2.0); Grade 4 neutropenia lasting for more than 4 days, Grade 4 anemia and thrombocytopenia, Grade 3 neutropenia accompanied fever (⩾38ºC), and Grade 3 non-hematological toxicity (except for nausea, appetite loss, general fatigue). Maximal Tolerated Dose (MTD) is determined when the incidence of critical toxicity exceeds 50% at a certain dose level.
Results: MTD was dose level 2: docetaxel 60 mg/m^2, cisplatin 15 mg/m^2, and 5-fluorouracil 800 mg/m^2/day. DLTs were diarrhea on level 1, and febrile neutropenia, diarrhea, and stomatitis on level 2. The major toxicity were Neutropenia (Grade 3 and 4, 56%), Leukocytopenia (Grade 3, 44%), Anemia (Grade 3, 11%), Diarrhea (Grade 3, 33%) and stomatitis (Grade 3, 11%). The overall response rate was 44.4% and recommend dose's response rate was 66.7%.
Conclusions: The recommended dose of docetaxel in this study was determined to be 50 mg/m^2. This combination chemotherapy of recommended dose appeared to be highly active with a response rate of 66.7% and to have acceptable toxicities. Phase II multicenter study has already started.

774 PUBLICATION

Epirubicin, cisplatin and capecitabine for advanced biliary tract adenocarcinoma: a phase II study

S.H. Park[1], S.I. Lee[2], S.H. Han[1], J.N. Lee[3], S.M. Bang[1], E.K. Cho[1], J.H. Lee[1], D.B. Shin[1]. *[1]Gachon Medical School Gil Medical Center, Medical Oncology, Internal Medicine, Incheon, Korea; [2]Dankook University Hospital, Internal Medicine, Cheonan, Korea; [3]Gachon Medical School Gil Medical Center, General Surgery, Incheon, Korea*

Background: Advanced biliary tract cancers (BTC) are associated with a very poor prognosis. Although numerous chemotherapeutic agents have been tested, the role of palliative chemotherapy in BTC has not yet been clarified. New therapeutic strategies are thus needed to improve the efficacy and survival, and we designed this study with new effective drug combination.
Materials and Methods: Patients with recurrent or metastatic BTC received a combination of epirubicin 50 mg/m^2, cisplatin 60 mg/m^2 on day 1, and capecitabine 1,000 mg/m^2 twice daily as an intermittent regimen of 2 weeks of treatment followed by a 1-week rest. Treatment was repeated every 3 weeks.
Results: Of 42 patients registered (14 with extrahepatic and 14 with intrahepatic cholangiocarcinoma, 6 with gallbladder cancer, 8 with ampulla of Vater cancer), one patient withdrew his consent and never received protocol therapy. The median age was 57 years (range, 36–69) and 5 had Zubrod performance status of 2. Objective responses were, which maintained for a median of 7 months), observed in 15 patients (36%) with 10 stable diseases. With a follow-up duration of 16 months, the median survival time was 8 months (95% confidence interval, 5–10 months). In total, 177 chemotherapy cycles were delivered, with a median of 5 cycles per patient (range, 0–9). Toxicity was mainly myelosuppression and mucositis. One patient died of hepatic failure between treatment cycles. For all patients, response to treatment was positively correlated with survival.
Conclusion: This combination chemotherapy with epirubicin, cisplatin and capecitabine feasibly offered promising antitumor activity in patients with advanced BTC.

775 PUBLICATION

Irinotecan and gemcitabine (IrinoGem) combined with 3-D conformal radiation therapy for locally advanced pancreatic cancer

R. Epelbaum, E. Gez, A. Kuten. *Rambam Medical Center, Department of Oncology, Haifa, Israel*

Background: Chemoradiation for locally advanced pancreatic cancer may improve local control and long-term survival. The combination of irinotecan (Irino) and gemcitabine (Gem) (IrinoGem) is active in pancreatic cancer and has an acceptable toxicity profile (Rocha Lima et al, JCO, 2002). Both drugs are also radiosensitizers. Therefore, we conducted a phase I/II study to evaluate the feasibility and efficacy of IrinoGem combined with radiotherapy (RT) in patients (pts) with localized, unresectable pancreatic cancer.
Material and Methods: Pts received 2 induction cycles of Gem 1000 mg/m^2 and Irino 100 mg/m^2 administered on days 1 and 8 of each 3-week treatment cycle. This was followed by 3 cycles of low-dose IrinoGem with concurrent abdominal radiation. Gem was administered at a fixed dose of 300 mg/m^2 and doses of Irino were escalated in successive cohorts from 20 mg/m^2 to 50 mg/m^2, by increments of 10 mg/m^2. RT was delivered by 3-D conformal technique to the pancreas and lymphatic drainage at 1.8 Gy daily fraction to a dose of 50.4 Gy.
Results: Sixteen pts entered the study between 11/2002 and 1/2004. Their median age was 66 y (range, 48–80 y) and performance status was 1/2 in 10/6 pts. All pts received 28 induction cycles and 11 pts continued with 33 cycles combined with RT. Treatment was stopped during the induction phase in 5 pts (toxicity 1, stent complications 1, refusal 1, tumor progression 2). Grade III-IV adverse events were diarrhea, vomiting, fatigue and mucositis in 5/16 (31%) pts during the induction phase and fatigue in 1/11 (9%) pts receiving concurrent chemotherapy and RT. There was no grade III-IV hematological toxicity. Thirteen pts were eligible for efficacy. Nine pts (70%) achieved clinical benefit response (CBR). One pt (8%) had an objective partial response, 7 pts (54%) had stable disease and 5 pts (38%) progressed, 2 of them during the induction phase. Release of major vessels encasement by the tumor was noticed in 2 pts, and one of them underwent R0 pancreatectomy. Median time to tumor progression was 6 m (range, 1–32+ m) and overall survival ranged from 2 to 32+ m, with a median of 13 m. Five pts are alive 1 y (1 pt), 2 y (3 pts) and 3 y (1 pt) after start of treatment.
Conclusions: This schedule of IrinoGem and RT is well tolerated and can provide CBR and disease control in pts with localized, unresectable carcinoma.

776 PUBLICATION

Phase I/II study of S1 plus docetaxel in patients with advanced or recurrent gastric cancer

D.Y. Zang, J.S. Ahn, J.Y. Jeong, J.H. Kwon, J.H. Kim, H.H. Song, H.J. Kim, Y.I. Park. *Hallym Medical Center, Internal Medicine, Anyang, Korea*

Background: S1 and docetaxel (TXT) show significant single-agent efficacy in gastric cancer and are synergistic in vivo studies. We performed a phase I/II study of S1 and docetaxel combination chemotherapy to determine the maximum-tolerated dose (MTD), recommended dose (RD), and efficacy in unresectable or recurrent gastric cancer.
Methods: Docetaxel was administered intravenously on day 1 and S1 was administered orally on days 1–14. Treatment was repeated every 3 weeks. Doses of each drug in the phase I study were as follows: TXT/S1- level 1 60/60; level 2A 60/80; level 2B 75/60; level 3 75/80 (mg/m^2). Phase II study is being conducted with RD based on the phase I study.
Results: Fifteen patients (median age 52) were enrolled in this phase I study and 9 patients (median age 52) were enrolled in this phase II study. No dose-limiting toxicities (DLTs) occurred at level 1, 2A, and 2B. At level 3, 2 of 3 (66.7%) patients developed DLTs (1 patient: grade 4 neutropenia with fever, 1 patient: grade 4 neutropenia with grade 3 stomatitis). Therefore, the dose at level 3 was determined as the MTD and the dose at level 2B was determined as the RD. The response rates of the phase I study were as follows: level 1 0% (0/3); level 2A 33.3% (1/3); level 2B (RD) 66.7% (4/6); level 3 66.7% (2/3). The response rate of the phase II study was 66.7% (4/6 evaluable patients: 1 CR, 3 PR, 1 SD, and 1 PD). Two patients (age 66 and 64 years old) developed fatal toxicity (grade 4 neutropenia with fever and shock) during the phase II study. The phase II study was well tolerated by the other 7 patients (all except 1 patient were younger than 60 years old). Additional phase I study with level 2A for the patients older than 60 years (n = 3) was conducted. No DLTs occurred at this level and the toxicities were easily manageable.
Conclusion: Level 2B (TXT/S1 at 75/60 mg/m^2) for the younger (<60 years old) patients and level 2A (TXT/S1 at 60/80 mg/m^2) for the older patients are the RD of this combination chemotherapy. This combination regimen showed a high response rate and tolerable toxicities in patients with advanced or recurrent gastric cancer. The phase II study is now under way.

777 PUBLICATION

Salvage surgery after failure of oncologic therapy for anal cancer

T. Hølmebakk[1], J.N. Wiig[1], E.H. Wanderås[2], K.-E. Gierkscky[1]. *[1]The Norwegian Radium Hopital, Department of Surgical Oncology, Oslo, Norway; [2]The Norwegian Radium Hospital, Department of Oncology, Oslo, Norway*

Background: After primary oncologic therapy for epidermoid anal cancer some 20%-30% will have either residual disease or experience locoregional recurrence. Extensive surgical resection remains the only treatment with a possible curative outcome in these cases. We report the results in patients operated in our institution.
Material and Method: Retrospective assessment of patients operated for cure with abdominoperineal resection (APR) for residual or recurrent epidermoid anal cancer after primary oncologic therapy from 1990 through 2003.

Results: During the period 243 patients were treated with combined radiochemotherapy (228) or radiotherapy alone (15) for epidermoid anal cancer. Fifty (21%) patients had an incomplete response or experienced locoregional recurrence. Of these, 27 patients underwent APR with curative intent, 16 for residual and 11 for recurrent disease. There were 17 women and 10 men, median age 60 (39–85) years. Residual disease was more frequent among men than among women (9/10 vs. 7/17), $p = 0.018$. Primary reconstruction with a myocutaneous flap was performed in seven cases. R0 was achieved in 20 (74%) patients; R1 in the remaining 7 (26%). Major complications, including one postoperative death (4%), were recorded in 18 (67%) patients, protracted perineal healing being the most common (13 patients, 48%). Follow-up was median 33 (0–131) months. Estimated crude five-year survival postsalvage was 43%. There was no statistically significant difference in survival between patients with residual and recurrent disease, R0 and R1 resections, women and men, but patients aged <50 years fared better than those aged ⩾50, $p = 0.0017$. Delayed healing did not influence survival. Postsalvage locoregional recurrence was recorded in 9 (34%) cases, irrespective of primary tumour size, R-stage and residual or recurrent disease with a median delay of 10 (1–59) months. Estimated five-year disease-specific survival was 59%.
Conclusions: Salvage surgery for failure after oncologic therapy for epidermoid anal cancer offers a fair hope of long-time survival, but complications are considerable. In our study no single patient-, disease- or treatment-related factor was predictive of survival or locoregional recurrence except better survival among the youngest patients.

778 PUBLICATION

Incidence of gastrointestinal stromal tumor: a retrospective study based on immunohistochemistry and mutational analysis

C. Tzen[1], J. Wang[2], Y. Huang[3], P. Lin[4], M. Wang[2], G. Lai[4], C. Wu[4]. *[1]Mackay Memorial Hospital, Department of Pathology, Taipei, Taiwan; [2]Novartis (Singapore) Pte. Ltd., Asia Pacific, Head of Medical Affairs, Singapore, Singapore; [3]Novartis (Singapore) Pte. Ltd. Asia Pacific, Regional Medical Advisor, Singapore, Singapore; [4]Mackay Memorial Hospital, Department of Medical Research, Taipei, Taiwan*

Background: To determine the incidence of gastrointestinal stromal tumor (GIST) is important to health care providers regarding the availability of imatinib mesylate (Glivec, Novartis Pharma, Basel, Switzerland), a remarkably effective therapeutic agent for GISTs. In this study, we aimed to determine the incidence of GIST based on the recently refined diagnostic criteria, particularly the CD117 immunostaining and mutation analysis of *KIT* and *PDGFRA* genes.
Material and methods: After reviewing 17850 surgically excised GI lesions during 1998–2004, immunohistochemical analysis for CD117 expression was performed for all mesencheymal tumors. Among them, every CD117-negative mesenchymal tumor was further subjected to mutational analysis for *KIT* and *PDGFRA* exons. Diagnosis of GIST was based on morphologic context, CD117 expression and *KIT*/*PDGFRA* mutation. Based on the percentage of GI cancer patients in Taiwan who were diagnosed and treated in our hospital, we estimated the incidence of GIST in Taiwan from the annual incidents of GIST patients diagnosed and treated in our hospital.
Results: Approximately 4.72% of patients with malignancies of the GI tract in Taiwan were surgically treated in our hospital. The average of newly diagnosed and surgically treated GIST patients in our hospital was 14.33 cases per year. Excluding incidentally identified GISTs by autopsy or endoscopy, the estimated number of GIST patients in Taiwan is 303.60 annually.
Conclusions: GIST is a rare tumor with an annual incidence of at least 13.74 per million Taiwanese. Approximately a quarter of GISTs are not correctly diagnosed if immunohistochemistry and mutation analysis are not employed.
Keywords: Gastrointestinal stromal tumor (GIST), CD117-negative GIST, incidence

779 PUBLICATION

Phase I trial of capecitabine and gemcitabine with concurrent radical radiotherapy in locally advanced pancreatic cancer: interim results

T. Leong[1], M. Michael[2], V. Ganju[3], T. Price[4], A. Strickland[5], M. Jefford[2], S. Ngan[1], J. Zalcberg[2]. *[1]Peter MacCallum Cancer Centre, Radiation Oncology, Melbourne, Australia; [2]Peter MacCallum Cancer Centre, Medical Oncology, Melbourne, Australia; [3]Frankston Hospital, Oncology, Frankston, Australia; [4]Queen Elizabeth Hospital, Oncology, Adelaide, Australia; [5]Monash Medical Centre, Oncology, Melbourne, Australia*

Background: Primary chemoradiation is commonly used for the treatment of patients with locally advanced, unresectable pancreatic cancer. The current standard regimen combines 5-fluorouracil with radiotherapy (RT). However, given the disappointing results of recent randomised trials utilising this regimen in the adjuvant setting, there is a need to investigate newer systemic agents with RT. The combination of capecitabine (Cap) (Xeloda®) and gemcitabine (Gem) has demonstrated activity in advanced pancreatic cancer and both agents are potent radiosensitisers. The aim of this phase I trial was to determine the MTD of Cap combined with Gem plus concurrent RT.
Material and methods: Eligible patients (pts) had unresectable, locally advanced pancreatic cancer based on imaging or laparotomy findings, adenocarcinoma histology, adequate organ function and ECOG PS 0–1, no prior RT or chemotherapy. During RT, Gem was escalated from 20 to 50 mg/m^2/day IV (given days 1 and 4 of each week of RT), and Cap was escalated from 800 to 2000 mg/m^2/day (given daily in 2 divided doses, days 1–5 of each week of RT) in 7 dose levels. RT consisted of 50.4 Gy/28 fractions/5.5 weeks using conformal techniques. Three patients were entered to each dose level and if 1 of 3 patients had a dose limiting toxicity(s) (DLTs) the cohort was expanded to 6 patients. DLTs were based on treatment related toxicities and treatment interruptions.
Results:11 patients have been accrued to date: stage I (3 pts), stage II (5 pts), stage III (3 pts). Dose level 1: Cap/Gem; 800 mg/m^2/day / 20 mg/m^2/day (3 pts). Dose level 2: 1000 / 20 (3 pts). Dose level 3: 1300 / 30 (5 pts). Following chemoradiation, 3 patients (27%) had a partial response, and 6 patients (55%) had stable disease. No DLTs were observed on dose levels 1 and 2, while 2 DLTs were observed on dose level 3; grade 3 dehydration (1 pt) and grade 3 diarrhoea (1 pt). Dose level 2 was declared the recommended dose level and is being expanded to a total of 15 patients. No grade 3 or 4 haematological toxicities.
Conclusions: The addition of capecitabine and gemcitabine to radiotherapy was feasible and generally well tolerated. For future trials capecitabine 1000 mg/m^2/day and gemcitabine 20 mg/m^2/day is the recommended dose when combined with 50.4 Gy of radiotherapy. Accrual continues and further results will be updated.

780 PUBLICATION

High serum level of neuron specific enolase indicates the histological typing of pancreatic and hepatobiliary neuroendocrine tumors as poorly differentiated neuroendocrine carcinomas

C. Morizane[1], N. Hiraoka[2], Y. Takahashi[2], T. Okusaka[1], H. Ueno[1], M. Ikeda[1], M. Najima[1], T. Hirokawa[1], T. Ogura[1]. *[1]National Cancer Center Hospital, Hepatobiliary and Pancreatic Oncology Division, Tokyo, Japan; [2]National Cancer Center Research Institute, Pathology Division, Tokyo, Japan*

Object: This study investigated simple, useful, and surrogate markers for predicting the histological differentiation grades of pancreatic and hepatobiliary neuroendocrine carcinomas (NECs).
Patients and Methods: We retrospectively studied 40 patients with malignant pancreatic or hapatobiliary NECs who admitted to the Hepatobiliary and Pancreatic Oncology Division, National Cancer Center Hospital, Tokyo, Japan, between 1991 and 2005. Original sites of the tumors were as follows; pancreas (n = 27), liver (1), bile duct (1), gallbladder (6), ampulla of Vater (2), and duodenum (2). 38 patients had metastatic disease. Pathological specimens were obtained from 32 patients by aspiration biopsy and from 8 patients by surgical resection, all of which were pathologically diagnosed according to WHO classification for pancreatic endocrine tumor (WHO, 2000). We evaluated several clinical factors if they correlate with the histological differentiation grades of tumors. In addition, we analyzed the relationship of serum neuron specific enolase (s-NSE) and other clinical factors in 33 patients, who received systemic chemotherapy in the 40 patients.
Results: Histopathological diagnoses of the tumors were well-differentiated NECs in 17 tumors and poorly differentiated NECs in 23 tumors. Tumors from all of the 10 patients with high levels of s-NSE (⩾50 ng/ml) were classified as poorly differentiated NECs. S-NSE value (⩾50 ng/ml or not) was strongly and significantly correlated to histological differentiation grades of tumors ($p = 0.0006$). But performance status, primary tumor site, number of metastatic tumor site, and intensity of immunohistochemical expression of NSE, chromogranin A, synaptophysin and CD56 in tumor cells were not correlated to the differentiation grades of tumors. Patients with high levels of pre-treatment s-NSE responded more frequently against the chemotherapy (5 of 12, 42%) than patients with low levels (<50 ng/ml) of pre-treatment s-NSE (1 of 19, 5%; $p = 0.02$). Patients with high levels of s-NSE also showed significantly shorter survivals than patients with low levels of s-NSE on univariate analysis (median survival time; 5.2 versus 12.2 months, $p = 0.0019$).
Conclusion: High s-NSE level is a good indicator to specify the tumor as poorly differentiated NEC occurred in pancreas and hepatobilliary tract. It is also suggestive of the tumor being highly sensitive to chemotherapy but aggressive in clinical course.