slight BE was seen in KE-6. When 10% HSV- tk+ cells were mixtured, about 50% of cells were killed in KE-8. All-trans-retinoic acid enhanced the GJIC and the BE by around 30% in KE-6. Conclusion: Our results suggest that Cx expression in cell-cell contact area is indispensable to BE induction in HSV-tk/GCV gene therapy. We can expect considerable effect of this gene therapy only for esophageal cancer expressing GJIC capacity. This gene therapy might become enough efficacious with Cx gene induction or up-regulation of GJIC by adequate chemicals,

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A comparsion of different techniques in VX2 tumor cell implantation

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Introduction/Purpose: The liver might harbor primary tumors and is the most common site for metastases from gastrointestinal tumors and malignant melanoma. Early detection or exclusion of a neoplasm is important for appropriate treatment. The authors compared four methods for tumor implantation into the rabbit liver for experimental purposes.

Methods: Fifty-five New-Zealand white rabbits, each weighing about 2.8-3.2kg, were used for the experiment. The rabbits were divided into 4 groups. Four different implantation methods were used to induce VX2 carcinomas respectively. In group one (n=10), tumor cells were directly injected into rabbit liver. In group two (n=19), we used alcoholic cotton swap pressed on the injected site after injection. In group three (n=16), we injected agarose to the needle track after the tumor cells suspension was implanted to prevent cancer seeding. In group four (n=10), we directly transplanted 1 mm3 of the tumor block into both the left and right lobe of the rabbit liver. The growing of the tumor cells were evaluated by CT scan after two weeks of inoculation.

Results: The successful inoculation was defined as no tumor seeding in the needle tract, peritoneum, and subcutaneous area. The successful rate for the four groups (I, II, III, and IV) were 10%, 32%, 88%, and 92% respectively. Agarose injection followed tumor cells suspension injection has comparable success rate as that of direct tumor block transplantation.

Discussion/Conclusions: With highly successful implantation rate, direct injection followed by agarose prevention is a convenient technique and is very useful when multiple implantation sites are demanded.

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Phase I/II clinical trial on the combination chemotherapy with CPT-11 and the new oral anticancer drug S-1 for advanced gastric cancer (AGC)

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Purpose: The purposes of this study is 1) To decide the recommended doses of CPT-11 in this combination chemotherapy, 2) To determine the side effects and safety of this combination therapy; 3) To evaluate the effectiveness, antitumor effect of this combination therapy for Advanced Gastric Cancer (AGC). Methods: Patients with AGC and chemotherapy-naive were entered this study. CPT11 was administered intravenously over 90-min on day 1 and day 15. S-1 was orally given from day 1 to day 14, twice a day after breakfast and supper.We established 3 dose escalation levels. While the dose of S-1 was determined, as just mentioned, the dose of CPT-11 was increased from 100 mg to 125 mg, and then to 150 mg. Results: Fifteen patients entered this study.Side effects observed as non- hematological toxicity (HT) were all mild, classified as grade 2 or lower, except for grade 3 non-HT observed at level 1 and grade 3 dermatitis at level 2.As for HT, grade 4 neutropenia occurred in one patient at level 1 and in 2 at level 2, but these side effects were within a tolerable range in the others.Then MTD has not yet been reached. The antitumor effect was observed in 3 patients at level 1, including one CR case, and 3 PR cases were observed at level 2. Thus a 50% efficacy rate was obtained. Conclusion: At the present time, although the clinical trial on this combination chemotherapy has been up to level 3, a 50% response rate, including one CR case, has been obtained, indicating that this regimen is effective in the treatment of AGC. Additionary, pharmacokinetics studies were performed.This study is now ongoing.

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Gemcitabine (G) and cisplatin (C) in the treatment of locally advanced and/or metastatic pancreatic carcinoma

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Purpose: G, an active agent in pancreatic cancer, has shown synergistic activity with C. We evaluated the efficacy and toxicity of the G plus C combination in patients with locally advanced unresectable and/or metastatic pancreatic carcinoma.

Methods: Inclusion criteria included: adults with advanced pancreatic carcinoma, measurable disease, no prior chemotherapy, ECOG performance status (PS) less than or equal to 2, adequate renal and liver function, good bone marrow reserve, life expectancy greater than or equal to 12 weeks, and informed consent. G 1250 mg/m2 was administered on days 1 and 8 with C 70 mg/m2 on day 1 every 3 weeks.

Results: From June 1997 to March 2001, 31 patients (21 males, 10 females) were enrolled with a median age of 56 years (range 34-71);. 17 patients had metastatic and 14 had locally advanced disease. At the time of the analysis, all patients were evaluable for toxicity and 28 were evaluable for response. Complete response (CR) was achieved in 2 (7.1%) patients and partial response (PR) in 7 (25%) patients, for an overall response rate (CR+PR) of 32.1%; 8 (28.6%) patients had stable disease and 11 (39.3%) had progressive disease. Clinical benefit response (based on reduction of analgesic consumption, increase in weight, and improvement of PS) was noted in 21 (67.7%) patients. Overall survival is 8 months. A total of 97 cycles was administered, with a median of 3.1 cycles (range 1-6). Severe toxicities (NCIC grade 3/4) evaluated over 97 cycles were thrombocytopenia in 8%, vomiting in 12%, anemia in 5%, and neutropenia in 2% of patients.

Conclusions: The combination of G and C is well tolerated and shows promising activity in pancreatic cancer, and confers a clinical benefit for most of the patients.

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Chemoradiation with gemcitabine ('gemzar') in the treatment of biliopancreatic cancer: a phase I study

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Purpose: Aim of this study was to establish the maximal tolerated dose (MTD) of gemcitabine (once weekly) that could be safely administered when combined with radiation in advanced biliopancreatic malignancies; moreover to assess clinical and pathological response rate.

Material and Method: 15 patients (M/F: 9/6; median age: 63.4; pancreatic ca: 10 pts, biliary ca: 5 pts; T4N0: 9 pts, T3N0: 4 pts, T4N1:2 pts) entered into the study. Five patients were treated with chemoradiation after radical surgical resection. Eligibility criteria included: disease limited to the local regional area without evidence of liver or distant metastasis, age less than 75, ECOG performance score 0-2, WBC > 4000, PLT >100.000, Hb > 10.

External beam radiation was delivered with 9-10 MV photons by using a three-field technique. The prescribed external beam dose (ICRU 50) was 50.4 Gy. The initial dose of Gemcitabine was 100 mg/m2 administered as a short intravenous infusion once a week. Three patients were treated at each dose level and if no grade 3-4 WHO toxicity (considered as DLT) was recorded, the dose of the drug was escalated in increments of 50 mg/m2 till MTD was established.

Results: All patients were evaluable for acute toxicity. Fourteen patients completed the planned course of chemoradiation without interruptions. There were no treatment-related deaths. No DLT occurred at the first 4 dose levels (100 mg/m2 -250 mg/m2).

At the 5th dose level (300 mg/m2), 3 patient experienced DLT: 1 grade 3 gastrointestinal toxicity, 1 uncomplicated grade 3 leukopenia and 1 grade 3 change in liver biochemistry tests.

In addition, all 10 patients unresected were evaluated for response, of whom 4 had PD (1 local; 2 distant; 1 local and distant) and 6 had NC.

Conclusion: In conclusion, gemcitabine concomitant with pelvic radiotherapy has allowed out-patient administration with manageable toxicity. The main drug-related toxicities were gastritis, leukopenia and increased level of serum transaminases. Based on this study, it appears that the MTD for weekly short infusional gemcitabine combined with radiation is 250 mg/m2. Further studies aimed to improve the response rate after chemoradiation are needed. Moreover, different infusion modality, like continous infusion of gemcitabine, should be tested more accurately.