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A prospective randomized phase III trial of 5-fluorouracil and cisplatin (FP) versus epirubicin, cisplatin, and 5-fu (ECF) in the treatment of patients with previously untreated advanced gastric cancer (AGC)

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Purpose: Combination chemotherapy of ECF regimen has known one of the active regimens in AGC. But, to date, no standard regimen for AGC has existed. We conducted a randomized phase III study to evaluate the efficacy and toxicities of FP and modified ECF regimen with previously untreated advanced AGC with measurable lesion.

Methods: Patients were allocated to receive either FP (5-FU 1,000 mg/m2 IV for 6 hours on days 1 to 5, and cisplatin 60 mg/m2 IV on day 1) or ECF (epirubicin 50 mg/m2 on day 1, cisplatin 60 mg/m2 on day 1, and 5-FU 1,000 mg/m2 IV for 6 hours on days 1 to 5) every 4 weeks.

Results: From Mar 1997 to Apr 2000, total 121 patients (pts) were enrolled in this study; 60 pts were randomly assigned to FP and 61 to ECF group. One pt was ineligible. The main pts characteristics were comparable between groups FP and ECF: median age 56.5 vs. 55 years, male/female 42/18 vs. 45/15, performance status 0-1 88.3% vs. 90%, locally advanced diseases/metastatic disease 3/57 vs. 3/57, and liver metastasis 47% vs. 53%. Total number of completed cycles was 199 (192 evaluable) in FP and 214 (208 evaluable) in ECF arm. Response was evaluabe in 53 pts in both arm and was observed in 20 pts (20 PR; RR 37.7%) for FP arm and in 22(22 PR; 41.5%) for ECF arm (p=0.66). There were no significant differences between the FP and ECF arms in the time to progression (median 3.9 vs. 4.4 months) or overall survival (median 7.3 vs. 8.5 months). Toxicity grade 3-4 for FP vs. ECF group included leukopenia (10.0% vs. 25.5% pts; p=0.02), thrombocytopenia (6.7% vs. 12.5%; p=0.31), mucositis (3.3% vs. 33.8%; p=0.01), nausea/vomiting (11.6% vs. 16.9%; p=0.41), and diarrhea(2% vs. 2%), respectively.

Conclusion: This trial showed that a combination of modified ECF regimen with this schedule did not showed any advantage over FP regimen in terms of response, survival and toxicity profiles.

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Treatment of locally advanced hepatocellular carcinoma (HCC) by hepatic intra-artery-chemotherapy (IACT): a pilot study

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Purpose: This study was done to assess whether IACT may be helpfull in locally advanced HCC.

Methods: 24 patients (pts) (mean age 69 range 48-80) with biopsy proven HCC and Child-Pugh A or B stages liver cirrhosis were enrolled. 18 had HCV related liver cirrhosis, 2 HBV related, 3 alcohol related and 1 cryptogenic form. 14 pts had no other treatment before IACT because of late diagnosis. All had US and spiral TC and underwent surgery for cholecistectomy and to implant a port a cath into gastroduodenal artery after angiografy. Treatment: 2 weeks interval schedule (8 pts): Folinic acid was infused (100 mg/mq) over 2 hours, followed by 5-FU 300 mg/mq in bolus and then by 5-FU 500 mg/mq infusion over 22 hours. Each course was repeated starting from a dose of 350 mg/mq and increasing until a maximun of 550 mg/mq. 1 Week interval schedule (16 pts): Folinic acid 100 mg/mq over 2 hours followed by 5-FU 250 mg/mq and increasing the dose until 550 mg/mq. Treatment was repeated when had good tolerability and until no evidence of disease or progression. No difference in response or toxicity were shown between these two schedules.

Results: Complication and toxicity were due mainly to surgery and handling of the port a cath. Overall median survival estimated from the diagnosis was 26,5 months (range 8-117) and 19 months (range 4-83) from the beginning of therapy. The response rate was: 13/19 evaluable pts had a major rsponse (2CR, 11PR) (54%) with a median time to progression of 15 months, 4 pts showed PD, 2 pts had SD. There was a significant advantage for pts with cirrhosis stage A as compared with those in stage B (p<0.005) considering the overall survival either from the biginning of chemotherapy or from diagnosis.

Conclusion: This pilot study shows that pts with locally advanced HCC and liver cirrhosis can be treated successfully with folinic acid and 5 FU by intrahepatic artery infusion.

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Comparison of the efficacy and tolerability of ZD9331 with gemcitabine in locally advanced or metastatic pancreatic cancer: phase II/III trial

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Introduction: Novel chemotherapeutic agents are required to improve the survival and progression outcomes of patients with pancreatic cancer. This study compares the efficacy and tolerability of ZD9331, a novel antifolate, with gemcitabine, the current standard treatment for this tumour type.

Methods: A total of 55 chemonaive patients with histologically or cytologically proven locally advanced or metastatic pancreatic cancer were enrolled in the trial. Patients (pts) were randomised to receive ZD9331 (n=30) or gemcitabine (n=25). ZD9331 (130 mg/m2) was given as a 30-min iv infusion on days 1 and 8 of a 21-day cycle. Gemcitabine (1 g/m2, iv infusion) was given once-weekly for 7 weeks (wks), followed by 1 wk rest, then on days 1, 8 and 15 of a 28-day cycle. The primary endpoint of the study was time to death (TTD). Secondary endpoints included tolerability and objective tumour response.

Results: The median survival time was longer for pts receiving ZD9331 compared with gemcitabine treatment (TTD, 152 and 109 days, respectively), with a higher proportion of ZD9331 pts alive at the end of the trial (13.3% vs 8% for gemcitabine). The median time to progression was also longer for pts receiving ZD9331 (70 vs 58 days for ZD9331 vs gemcitabine pts). Partial responses were confirmed in 1 ZD9331 pt and 2 gemcitabine pts. However, a higher proportion of ZD9331 pts had stable disease (33.3% vs 24% for gemcitabine treatment). Overall, more ZD9331 pts than gemcitabine pts withdrew from therapy due to adverse events (AEs) (33.3% and 20%, respectively). The most common AEs with ZD9331 were nausea/vomiting and asthenia but these were generally mild to moderate: grade 3/4 adverse events were uncommon and comprised neutropenia (5 pts), thrombocytopenia (4) and leucopenia (3). Three patients receiving gemcitabine had grade 3/4 anaemia. Three ZD9331 pts and 2 gemcitabine pts died due to AEs. Two of the deaths in the ZD9331 group were considered to be drug-related (sepsis and myelosuppression, respectively) and this led to the early termination of the trial at the data summary stage.

Conclusions: Although there was a higher withdrawal rate from ZD9331 therapy due to toxicity, the promising preliminary efficacy data indicate that ZD9331 treatment may have a role in the treatment of locally advanced or metastatic pancreatic cancer.

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Effect of extensive lymph node dissection in surgical treatment of early gastric cancer

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Purpose: Early gastric cancer (EGC) has been defined as a gastric carcinoma confined to mucosa or submucosa, regardless of lymph node status (T1NX). Our objective was to evaluate the long-term benefit of extensive lymph node dissection in the treatment of EGC patients.

Method: From 1987 to 2000 we had surgically treated 169 patients with EGC (Tis-32, T1m-66, T1sm-71). Limited resection was performed in 2 patients, 2/3 gastric resection in 2, subtotal resection in 104 (proximal-4, distal-100), gastrectomy-59, gastrectomy of gastric stamp-2. 111 patients were operated with D0 (n=8) and D1 (n=103) lymph node dissection, 18±D2 resection, 21-D2 resection with dissection of lymph node of hepatoduodenal zone (D2 +_12), 19-with D3 lymph node dissection.

Results: Hospital mortality rate was 1.2% (2 patients died in D1 group). Postoperative morbidity rate was 28.8% in D0-D1 group and 30.2% in D2-D3 group (p>0.05). Lymph node metastases were revealed in 14 patients (8.28%). There are no lymph node metastases of EGC Tis; the incidence of EGC T1m metastases is 4.55%, EGC T1sm-15.49%. 11 patients had metastases only in the perigastric regional node (N1); 3 had metastases in extraperigastric nodes in group _8, 10, 12; 1 of this 3 patients had metastases at the lymph node _12 (N3), the N1 and N2 nodes were clear. Higher metastatic incidence was in D2-D3 group (12.7%) compared with D1 group (6.3%). 5-year survival was statistically higher in N(-) EGC patients compared with N(+) patients (89.26±2.84%