(22) oesophageal (1) gastric (9) or OG junction (22) adenocarcinoma received up to 6 courses of E (50 mg/m2) C (60 mg/m2) and XEL at 3-weekly intervals. XEL was administered orally in an intermittent schedule (14 days treatment, 7 days rest period) at doses of 500 mg/m2 bd, 825 mg/m2 bd, 1000 mg/m2 bd, and 1250 mg/m2 bd in successive cohorts. Up to 6 evaluable patients were recruited into each dose cohort with no intra-patient dose escalation. Dose escalation occurred after 6 patients had completed at least 1 cycle of chemotherapy at the previous dose level. DLT was assessed on the first-cycle toxicity only. The MAD was 1250 mg/m2 bd with 2 of 5 patients experiencing DLT (grade 2 stomatitis [1], grade 3 diarrhoea with febrile neutropenia [1]). Cumulative toxicity for all cycles (n=140) (worst NCI-CTC grade per patient) included grade 4 oesophagitis (1 patient) grade 3 diarrhoea (5) grade 4 neutropenia with infection (7) grade 2 stomatitis (4) and grade 4 thrombocytopenia (1). Of 29 patients with evaluable disease there was 1 documented CR and 11 PR (41%). PK analyses (first cycle only) confirm absorption of capecitabine in patients with active OG cancer or previous OG resection with peak concentration of 291-9499 ng/ml, of DFCR from 701-9586 ng/ml, and of DFUR of 611-8948 ng/ml. A dose of 1000 mg/m2 bd capecitabine is recommended in combination with EC. This is tolerable and active and a randomised comparison with ECF is justified.

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## Multicenter phase II trial of first-line irinotecan (CPT-11) and gemcitabine (GMB) in patients with unresectable pancreatic cancer

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**Objectives:** GMB is considered as standard treatment of pancreatic cancer conferring a significant clinical benefit to the patients. CPT-11 is active in gastrointestinal malignancies. Based on preclinical data suggesting synergism between the two drugs and their different mechanism of action a multicenter phase II study was conducted in order to evaluate the tolerance and the efficacy of their combination.

**Patients and Methods:** Fifty-seven chemotherapy-naïve patients with advanced pancreatic cancer [median age: 65 years, F/M: 33%/67%, PS 0/1/2: 5/36/16, median involved sites/pt: 2] were enrolled. Patients received GMB (900 mg/m$^2$ over a 30-min infusion) on days 1 and 8 and CPT-11 (300 mg/m$^2$ over 1 h infusion) on day 8 every 3 weeks.

**Results:** All pts were evaluable for toxicity, 52 for response (intention-to-treat). Two (4%) CRs, 10 (19%) (ORR 23%; 95% C.I. 11.63%–34.53%) PRs, 18 (35%) SD and 22 (42%) PD were documented (intention-to-treat-analysis). The median duration of response is 3.25 months, the median TTP is 6.3 months and the median survival 8 months. Grade 3–4 neutropenia occurred in 24 (42%) pts and 9 (16%) of them developed febrile neutropenia; 3 pts died because of sepsis. Grade 3 anemia was observed in 2 (4%) pts and grade 3–4 thrombocytopenia in 7 (12%). Non hematologic toxicity included grade 3 diarrhea in 4 (7%) pts, grade 3 vomiting in 2 (4%), grade 3 fatigue in 8 (14%). The other toxicities were mild.

**Conclusion:** The combination of GMB/CPT-11 is a relatively active regimen for patients suffering from pancreatic cancer with acceptable toxicity.

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## Treatment of pancreatic endocrine tumours with adriamycin-streptozotocin association: evaluation of efficacy and prognostic factors of response and survival

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**Introduction:** Adriamycin-streptozotocin association has been considered as the chemotherapy of choice in the treatment of advanced pancreatic endocrine tumour (PET) until recently when a trial failed to confirm the efficacy of this chemotherapeutic regimen. Because of these conflicting results, we decided to present our experience of this specific therapeutic regimen in the treatment of advanced PET. The aim of our study was to assess retrospectively the objective response rate and survival of patients suffering from PET and treated by this association. Furthermore, we tried to determine prognostic factors of response and survival. Finally, we analysed the toxicity of this regimen.

**Material and methods:** between January 1995 and December 1999, we investigated retrospectively 45 consecutive patients suffering from advanced PET and receiving adriamycin-streptozotocin association. The chemotherapeutic protocol was adriamycin 50 mg/m2 day 1 and 21 and streptozotocin 500 mg/m2 day 1 to 5. This treatment was administered every 6 weeks(day 1= day 43). The patients were assessed every two months by radiological examination.

**Results:** there were 18 women and 27 men, median age 54 years. Fourty two of the 45 patients had metastases (liver 39/42, lymph nodes 18/42, peritoneum 3/42, others 12/42). Performance status was 0 in 34, 1 in 7, 2 in 3 and 3 in 1 of the patients. Sixteen patients have been previously treated by surgery, 11 by systemic chemotherapy, 4 by radiotherapy, 4 by chemoembolization, and 11 by somatostatin analogues. Sixteen of the 45 patients had partial response and seven had a minor response. The objective reponse rate was 35.6%[IC95%:0.22-0.49]. Several prognostic factors of response to chemotherapy have been isolated, especially previous chemotherapy (p=0.0033)or hepatomegaly (p=0.0156) which worsened the response to chemotherapy. Furthermore, previous chemotherapy (p=0.00835)or chemoembolization (p=0.00546) and hepatomegaly (p=0.05) were associated with a poor overall survival. Finally, the association was well-tolerated with 7 grade 3-4 digestive side effects (OMS classification)and 3 febrile neutropenia.

**Conclusions:** adriamycin-streptozotocin combination was well tolerated and associated with up to 35% of objective response rate, which confirm the results of the Mayo Clinic trial. Moreover, prognostic factors of response and survival isolated in our study could be interested to select patients who received this chemotherapeutic treatment.

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## Survival in the surgery of pancreatic tumours with vascular involvement

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The aim of the study is to evaluate survival time, with a retrospective analysis of a database of patients with pancreatic adenocarcinoma who underwent pancreatic and portal or mesenteric resection. In the period between January 1994 and December 1999 were admitted 74 patients affected by solid pancreatic adenocarcinoma (men 59%, women 41%). The diagnosis of vascular involvement was done with the angioscan, angiography or surgical exploration. Survival data were evaluated according to Kaplan Mayer, Wilcoxon Test was used to assess statistical differences between groups. The software was Statistical for Windows, version 4.0 Stadfot Inc., 1993. In this group, 59 patients were submitted to resection or palliative surgery, 5 had a diagnostic laparatomy and 10 medical therapy only. Of 59,in 33 cases pancreas underwent resection and, among these, 10 vascular resections were performed: 5 resection of the portomesenteric axis and direct end-to-end reconstruction and 5 marginal resections and direct suture. In 26 patients was performed a palliative operation. Histologic evidence of tumour cell infiltration of vessel walls was present in the majority of the resected specimens. Thirty-day mortality was 6.6% in the pancreatic resection without vascular involvement, 8.3% in vascular resection and 11.5% in the palliation. All patients were submitted to chemotherapy (5Fu and/or Gemcitabine) when required. Significant results were shown for the mean survival of 6,5 months for the vascular resections and 18.3 months for the pancreatic resections without vascular involvement (Wilcoxon P=0.02703, Cox P=0.042).The mean survival was also of 7 months for the surgical palliation and 6.8 months for the diagnostic laparatomy. Finally there was no significant survival time difference between palliation versus vascular resection, 7 and 6.6 month respectively, with the Wilcoxon test P =0.462 and the Cox test non significant.

**Conclusion:** Patients undergoing vascular resection have an uniformy poor outcome despite resection. The prognosis of these patients is dismal and corresponds to the prognosis with palliative nonresectional surgery. We believe that vascular resections can be safely performed and seems to improve the quality of life but needs further study in these high-risk patients.