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High-dose Folinic Acid, 5-Fluorouracil Bolus and Infusion in Advanced Pancreatic Adenocarcinoma: a Pilot Study

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MOST PATIENTS with pancreatic adenocarcinoma present with unresectable advanced disease. 5-Fluorouracil (5FU), streptozotocin and mitomycin-C have demonstrated limited antitumoral activity [1] and combined regimens did not improve results [2]. Folinic acid has been reported to enhance the activity of 5FU [3]. 5FU was given as a continuous infusion with an added bolus in a 2-day/2-week schedule to maximise 5FU doses and to avoid the cumulative toxicity of 5-day consecutive regimens. This combination has been used with low toxicity in advanced colorectal [4] and gastric cancers [5].

20 previously untreated patients (13 males/7 females, mean age: 53 years, range 30–76) with advanced non-resectable measurable histologically confirmed pancreatic adenocarcinoma entered the study. They received a 2-h infusion of folinic acid 200 mg/m^2, followed by 5FU 400 mg/m^2 bolus and a further 600 mg/m^2 in a 22-h infusion on days 1 and 2, every 2 weeks (LV5FU2). Performance status was 0 in 4 patients, 1 in 9, 2 in 5 and 3 in 2. 16 patients had liver metastases, 6 had peritoneal carcinomatosis, 5 had lymph node involvement and 3 had pleural or lung metastases. Extension and tumour size were evaluated by computed tomography scan prior to therapy. The first evaluation was made after 3 months and subsequently at 3-month intervals. Responders and stable patients continued on the same treatment until progression. Response was evaluated according to WHO criteria. Duration of response and survival were calculated from the beginning of treatment until progressive disease or death, respectively. Radiotherapy was given in patients with pain, as evaluated on distant metastases. The median follow-up time in October 1992 was 25 months.

Two partial responses (10.5%; 95% confidence interval: 0.1–24.6%) and six stabilisations (one minor response) (31.6%) were observed in 19 evaluable patients. Partial responses lasted 10+ and 12 months and the minor response lasted 17+ months. Median survival was 6 months, 4 patients were alive at 1 year. Treatment was well tolerated, grade 2 and 3 WHO toxicity was as follows: diarrhoea 2 patients, nausea and vomiting 3, mucocitis 2 and anaemia 2 patients. Of the stable patients and responders, performance status and symptoms improved in 3 patients, remained stable in 4 and worsened in 1.

The regimen is well tolerated but only achieved a 10% response rate and 6 months median survival. This agrees with two previous studies of 5FU/leucovorin which also reported poor results in advanced pancreatic cancer [2, 6]. Furthermore, no response was obtained in 6 patients with advanced pancreatic carcinoma treated with the same regimen [7]. The poor median survival led to a discontinuation of the pilot study. This combination is not recommended in the treatment of advanced pancreatic adenocarcinoma.

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Low Frequency of NF1 Gene Mutations in Malignant Gliomas

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DIFFERENT MUTATIONS of the NF1 gene have been described in patients with type 1 neurofibromatosis, an autosomal dominant disorder associated with cutaneous and subcutaneous tumours,

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