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Phase II trial of high-dose gemcitabine in patients with metastatic pancreatic adenocarcinoma

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Purpose: Although gemcitabine has shown superior antitumour activity than 5-FU in advanced pancreatic cancer (PC), further improvements are warranted To investigate if this goal might be achieved by dose intensification, the present phase II study was initiated.

Methods: Between 08/97 and 09/98, 38 consecutive patients with metastatic PC were entered in this trial. Treatment consisted of gemcitabine 2200 mg/m^2 given iv every 2 weeks for a duration of 6 months unless there was prior evidence of progressive disease.

Results: 28 pts (11 female, 17 male) are currently evaluable for response and toxicity assessment. Their median age is 65 (46–75) years, and their median Karnofsky performance status (KPS) 70% (50–100%). 20 (71%) were symptomatic at the time of initiating therapy.

A "clinical benefit response" (defined as a ≥50% reduction in pain intensity, ≥50% reduction in daily analgetic consumption, or ≥20% KPS score improvement for ≥4 weeks) was achieved in 7/20 (35%) symptomatic pts, and stabilization was noted in 6 (30%). Objective tumour responses (as assessed by serial CT-scans) occurred in 8 pts (28%), and 10 (36%) had stable disease. Median time to progression (≥4.5 mos) and median survival (≥6.5 mos) have not been reached yet. Therapy was generally well tolerated with a low incidence of severe (WHO grade 3) haematologic (21%) or other organ toxicities (11%).

Conclusions: Our findings suggest that high-dose gemcitabine is a tolerable and palliatively effective regimen for the treatment of pts with this otherwise chemorefractory fatal disease.

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Preoperative chemotherapy with weekly cisplatin plus continous infusion of fluorouracil and hyperfractionated radiation for esophageal cancer

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Purpose: In esophageal cancer, preoperative concurrent chemoradiotherapy is a promising approach, and accelerated hyperfractionated radiation increases local tumor control compared to standard radiation (Nishimura, 1994). We designed a phase II study to test cisplatin plus continuous infusion of fluorouracil plus concurrent hyperfractionated radiotherapy in squamous esophageal cancer.

Methods: From October 1996 to July 1998, 18 patients (p) were included. 15 were male and 3 female; mean age 58 (42–76). 3 p (16%) had >10% weight loss. Esophageal ultrasound-based staging revealed 4 p with stage II and 14 p with stage III. Treatment consisted of: cisplatin 30 mg/m^2, days 1, 8, 15; fluorouracil 300 mg/m^2 daily, continuous IV, days 1–21; radiation, 1.5 Gy bid, days 1–21, total dose 45 Gy. Resection was performed 3–5 weeks after chemoradiotherapy.

Results: All patients completed planned preoperative treatment. Grade 3/4 toxicities included esophagitis in 11 p (61%) and neutropenia in 3 p (16%); 9 p were hospitalized during the treatment and 5 p required parenteral nutrition. Of the 14 p eligible for curative resection, 13 p (72%) had all gross tumor removed. Six of 14 p (42%) had pathologic complete response, and 2 p had only microscopic residual. There were no treatment-related deaths. With a median follow-up of 17 months (range, 8–28), median survival has not been reached. 1- and 2-year survival rates are 70% and 58%. To date, 10 p (55%) remain alive without relapse.

Conclusions: In spite of a high incidence of esophagitis, this chemoradiotherapy combination has demonstrated a substantial activity with an encouraging 2-year survival in patients with resectable squamous esophageal cancer.

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Proliferative index and DNA content in precancerous conditions and adenomatous polyps of stomach

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Purpose: Gastric carcinogenesis is a multistep process, which develops on a background of precancerous conditions. The most prevalent precancerous condition is chronic atrophic gastritis, followed by intestinal metaplasia. Hyperplastic polyps are usually considered as non-neoplastic. Adenomatous lesions (flat and polyps) have been considered the only precursor lesions of gastric carcinoma. We evaluated the proliferative index and DNA content in these precancerous conditions and compared the results with those obtained in adenomatous polyps.

Methods: The immunohistochemical study of PCNA and evaluation of DNA content by image cytometry, were performed in 20 samples of normal gastric mucosa, 20 cases of superficial chronic gastritis, 20 cases of chronic atrophic gastritis with intestinal metaplasia, 8 hyperplastic polyps and 8 adenomatous polyps.

Results: In superficial chronic gastritis and atrophic gastritis, we observed a "superficialization" of cell proliferation. In intestinal metaplasia type III and in hyperplastic polyps we detected a high cellular proliferative index and some aneuploid cells. We found that the percentage of aneuploid cells in hyperplastic and adenomatous polyps (2.8% + 2.1% and 9.3% + 2.9%, respectively) was significantly higher ($p < 0.01$) than in normal gastric mucosa (0.1% + 0.3%). Similarly, the labelling index of PCNA was significantly higher ($p = 0.0001$) in hyperplastic and adenomatous polyps (47.6 + 8.9 and 63.9 + 7.6 respectively) than in normal gastric mucosa (14.3 + 4.8).

Conclusion: We found evidence supporting that the precancerous conditions share similar proliferative indexes and DNA content alterations as adenomatous polyps but less intense.

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Clinical pathway for the management of gastric cancer with peritoneal seeding

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Background: Patients evaluated for primary gastric cancer may have peritoneal carcinomatosis as a manifestation of stage IV disease. Strategies are needed to optimally palliate these patients and allow for an evolution of improved treatments. The purpose of this abstract is to review the information available in the literature and formulate a clinical pathway.

Methods: All papers and abstracts published over the last 30 years in the English literature were surveyed.

Results: Thirteen reports were reviewed concerning the results of treatment of patients undergoing palliative gastrectomy (1888 patients). Mean survival in months was more than doubled in all papers when patients underwent distal or total gastrectomy as compared to bypass or exploration only. Three papers included data regarding peritonectomy of peritoneal implants in addition to gastrectomy (120 patients). There was a statistically significant improvement in 5-year survival with complete cytoreduction in all reports. Eight reports focused on the use of perioperative intraperitoneal chemotherapy for patients having gastrectomy (714 patients). Patients with resectable stage IV disease had an increased likelihood to survive at 3 years after surgery with an odds ratio of 3.3 (confidence interval 1.7–11.0) and there were occasional prolonged survivors.

Conclusion: The gastric cancer literature suggests that palliative treatment of gastric cancer with peritoneal seeding may be improved by combining gastrectomy, peritonectomy, and perioperative intraperitoneal chemotherapy.

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Preoperative short-term radiotherapy of resectable gastric cancer: Complete 20-years follow up of a randomized trial

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Purpose: To determine the impact of preoperative short-term radiation therapy with a dose of 20 Gy given during 5 consecutive days on survival in gastric cancer patients, a prospectively randomized clinical trial was performed from 1974 to 1978.