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Letters

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Effective Intrahepatic Administration of Gemcitabine after Failure of Doxorubicin in Metastatic Breast Cancer

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GEMCITABINE, a novel nucleoside analogue, has shown activity as single agent in several solid tumours [1]. In locally advanced or metastatic breast cancer, a response rate of 25% has been reported using a dose of 800 mg/m^2 in primarily pretreated patients [2]. In first-line patients, a 40% response rate has been observed [3]. Due to its favourable toxicity profile, gemcitabine seems to be a suitable agent for the treatment of advanced breast cancer. The major side-effects of gemcitabine are mild haematotoxicity, elevation of transaminases and flu-like syndrome [4]. Although many clinical trials have been performed with gemcitabine for different tumours, there are no reports on the locoregional administration of this drug.

We report the case of a 70-year-old woman with liver metastases from breast cancer, who was treated with intrahepatic administration of gemcitabine. The patient was diagnosed for breast cancer in July 1993. She had a resection of the right breast, local radiotherapy and endocrine treatment with tamoxifen. In November 1995, she developed a single liver metastasis. An arterial port-a-cath system was implanted and the patient was treated with locoregional chemotherapy via the hepatic artery. First, she received seven cycles of 50 mg/m^2 doxorubicin and showed a partial response that lasted for only 3 months. Because of disease progression (appearance of new metastases in the liver), it was decided to treat the patient with a locoregional administration of 1250 mg/m^2 gemcitabine on days 1, 8 and 15 of a four-week cycle. The patient received four courses of treatment. A partial response was achieved, the duration being 5 + months at present. The patient had no treatment-related side-effects with gemcitabine.

Locoregional chemotherapy via the hepatic artery using gemcitabine thus seems a very attractive option. Based on the rapid elimination of gemcitabine with a half-life ($t_{1/2}$) of 8 min [5], a more favourable toxicity profile can be expected as with the standard intravenous route, while at the same time achieving high local concentrations.

In conclusion, our case shows that locoregional administration of gemcitabine is feasible, active—even in doxorubicin resistant cases—and very well tolerated. Intra-arterial administration of gemcitabine could also be an option for liver metastases from various sensitive tumours and for pancreatic carcinoma. Finally, we suggest the initiation of phase I dose-finding clinical trials for locoregionally administered gemcitabine.

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Post-transplant EBV-Associated Pancreas Carcinoma

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THE ROLE of EBV (Epstein-Barr virus) has been described extensively in the development of post-transplant lymphoproliferative disorders [1]. However, data on EBV-associated solid malignancies in organ recipients are rare. We describe a

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Table 1. *Results of PCR for viral DNA in tissue samples of the pancreas cancer, liver metastases, transplant kidney and native kidney*

	Pancreas carcinoma	Liver metastases	Transplanted kidney	Native kidney
EBV-DNA	positive	positive	positive	positive
CMV-DNA	negative	negative	negative	positive

patient who developed possibly EBV-associated pancreas carcinoma 2 years after renal transplantation.

A 47-year-old black male patient received an allogenic kidney transplant in 1992 after 6 years of haemodialysis because of end stage renal disease of unknown origin. The donor was seronegative for cytomegaly virus (CMV). EBV serology of the donor was not done. Serological testing of the recipient was consistent with past infections by EBV and CMV. Because of a moderate interstitial rejection, one course of high-dose prednisone was applied. No monoclonal or polyclonal antibodies were administered. Maintenance immunosuppression consisted of prednisone, azathioprine and cyclosporine.

In November 1994, the patient presented with abdominal pain. Diagnostic evaluation revealed a metastatic adenocarcinoma of the pancreas. Four weeks later, the patient died. Serological testing one week prior to death was negative for HIV, and consistent with past infections by EBV and CMV.

After autopsy, tissue samples of the pancreas carcinoma, liver metastases, transplanted and native kidneys were studied for EBV and CMV by *in situ* hybridisation (ISH) and qualitative polymerase chain reaction (PCR). Results of PCR are shown in Table 1. In all organs, ISH was positive for all EBV markers (nuclear antigen-1, -2 type A and B, and -3A, EBV encoded RNA 1, EBV receptor CD-21) in at least 30% of tumour cells, but not in stromal cells.

EBV-associated gastric cancer, colonic cancer and smooth-muscle tumours have been reported following organ transplantation [2, 3]. Pancreatic cancer is an unusual type of a post-transplant neoplasm. In a review of 3051 types of malignancy that arose in 2885 organ transplant recipients, there were only 25 (0.82%) cancers of the pancreas [4]. No post-transplant EBV-associated pancreas carcinoma has been reported so far.

Expansion of EBV occurs frequently in organ recipients and may persist without inducing malignant transformation even in non-immunosuppressed patients [1, 5]. Hence, the serological detection of EBV in a cancer patient does not prove the tumour to be EBV-related. However, we found EBV by ISH only in tumour cells, and not in stromal cells of our patient. This is evidence against a persistent generalised EBV expansion, and indicates that only tumour cells were infected by EBV that consecutively contributed to the malignant transformation.

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Impact of Histamine and Histamine$_2$ Receptor Antagonists on Quality of Life and Antitumour Responses: Results of a Pilot Trial

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HISTAMINE IN combination with histamine$_2$ receptor antagonists (H_2RAs), such as the common drugs cimetidine and ranitidine, is associated with marked clinical improvement in performance status, survival and investigator's estimates of quality of life in a study of 74 nursing home patients with cancer [1]. The average survival in the 31 treated patients (172 ± 113 days) was significantly longer than that of the 34 non-treated patients (26 ± 16 days). Six of the 31 treated patients showed responses including metastases in liver and lung. However, the study was not randomised and did not use a formal quality of life instrument. H_2RAs alone have been reported to benefit cancer patients with minimal cost and toxicity [2–6]. This study evaluated histamine and H_2RAs in the therapy of advanced cancer in a double-blind randomised trial with the primary endpoint of quality of life.

The trial was approved by the Committee on the Conduct of Human Research. 21 patients at the Medical College of Virginia Massey Cancer Center received ranitidine 300 mg by mouth twice daily and histamine 2.0 mg subcutaneously twice daily, or placebos for both drugs as previously reported by Burtin and associates [1], for 2 months or until progression of disease. Quality of life data were collected as the

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