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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Table 1. *Summary statistics of patients and the FLIC global score*

Day	Placebo ($n = 10$)		Histamine and H_2RAs ($n = 11$)	
	n	Global FLIC scores, Mean ± S.D.	*n*	Global FLIC scores, Mean ± S.D.
	Age 50–76 years, mean 63 years. Melanoma 4; colorectal 2; head and neck 1; non-small cell lung 1; lymphoma 1; renal 1 Progressive disease 9, no response 1		Age 31–63 years, mean 52 years. Non-small cell lung 2; rectal 2; renal 2; breast 2; gastric 1; adrenal 1; pancreas 1 Progressive disease 9, no response 2	
1	10	111 ± 10	10	107 ± 21
8	10	107 ± 17	8	114 ± 13
15	8	102 ± 20	9	114 ± 25
29	7	105 ± 16	8	112 ± 16
42	8	95 ± 29	4	120 ± 7
57	6	96 ± 28	4	120 ± 6

Results based on repeated measures analysis. For treatment, the *P* value was 0.21 for comparison; for day, the *P* value was 0.40; for treatment x day, the *P* value was 0.11.

Functional Living Index, Cancer (FLIC) [7] at 0, 7, 14, 28 and 56 days on treatment. An 'intent-to-treat' analytical format was followed, and all randomised patients who completed quality of life forms were included in the data analysis. A *P* value of ≤ 0.05 was considered statistically significant. Repeated measures analysis, using the PROC MIXED procedure in SAS, was done where patients and treatment were taken as random and fixed effects, respectively, in the model.

21 patients were treated during a 2-year period. Treatment and placebo group FLIC scores showed no change at baseline or during treatment (Table 1), but only half the patients were able to complete the FLIC as their disease progressed. The global FLIC scores of the treatment groups improved slightly, but the difference was small ($P = 0.21$ for global scores) and not statistically significant. No antitumour responses were seen in the 10 patients randomised to histamine and ranitidine. Accrual was slow, despite available patients, so the study was closed.

Our small trial was unable to confirm the results of Burtin and associates [1]. Physicians expressed reluctance to 'give up' on patients by giving them an unproven treatment (rather than additional chemotherapy), and to discuss the terminal nature of their patients' illness (as demanded by the written informed consent). Some physicians and patients expressed strong reluctance to undergo randomisation, although the therapy was not expected to cause toxicity and there were no good alternative therapies. Similar low rates of completion of quality of life studies have been reported in other trials [8, 9] and make quality of life problematic as an end-point for terminally ill patients. Even though our sample size was not large or homogeneous enough to rule out a response rate of 20%, the traditional threshold for responses [10], the lack of antitumour responses and lack of effect on quality of life make further trials unlikely.

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