An open-label phase I/II dose escalation study of the treatment of pancreatic cancer using lithium gammalinolenate.

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Abstract
There are currently no satisfactory treatments for inoperable pancreatic cancer. Median survivals for untreated patients are of the order of 100 days and, with one exception, no chemotherapy or radiotherapy regime has been found to produce a worthwhile extension of life with reasonably tolerable side effects. Gamma-linolenic acid (GLA) has been found to kill about 40 different human cancer cell lines in vitro without harming normal cells. The lithium salt of GLA (LiGLA) can be administered intravenously and a dose escalation study of a 10 day infusion followed by oral therapy in patients with inoperable pancreatic cancer was carried out in 48 patients in two centres. Peripheral venous infusion caused thrombophlebitis but this could be avoided by infusing via a central vein with appropriate heparinisation. Too rapid infusion caused haemolysis which could be avoided by slow dose escalation in the first few days and maintenance of plasma lithium below 0.8 mmol/l. Doses ranged from 7 to 77g/patient cumulatively delivered over 2-12 days. Other than the above described events there were no important side effects and patients felt well during the infusions. A Kaplan-Meier analysis showed that survival was not significantly influenced by which centre the patients were treated in, the sex of the patients or the presence or absence of histological confirmation. The presence or absence of liver metastases, the patients' Karnofsky scores and the dose of LiGLA had significant effects on survival from treatment. A Cox proportional hazards model revealed similar results: in both centres, in both sexes, and in patients with and without liver metastases according to the model the highest doses of LiGLA were associated with longer survival times as compared with the lowest doses. LiGLA deserves investigation in a randomised prospective study.

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