

disease, 1 patients had extensive disease with boney metastases. 2 of the 13 patients with limited disease had a small peripheral nodule detected on routine chest films. Only 2 patients had weight loss in the 6 months prior to the diagnosis. 5 patients were treated with local therapy alone (surgery 3, radiotherapy 1, surgery plus radiotherapy 1), 9 patients received systemic treatment (chemotherapy 5, chemotherapy plus radiotherapy 4). Median duration of cytostatic treatment was 17 months (3 - 39) with 3 of 9 patients receiving chemotherapy for less than 6 months. Chest radiotherapy doses varied from 2000 rads over 1 week to 7000 rads over 7 weeks. Only 1 patient received prophylactic cranial irradiation. 3 patients relapsed after initial treatment (surgery 1, radiotherapy 1, radiotherapy plus chemotherapy 1) after 27, 34 and 54 months. Median survival is 56+ months (27+ - 81+). Patients have been off treatment for a median of 41+ months (2+ - 75+).

We conclude that long term, disease-free survival can be achieved in patients with limited disease SCCL even with relatively short initial treatment.

PHASE I CLINICAL TRIAL AND PHARMACOKINETIC STUDY OF 5'-DEOXY-5-FLUOROURIDINE

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5'-deoxy-5-fluorouridine (DFUR) is a new fluorouridine analog lacking a 5'-hydroxyl group in the chemical structure of its pentose ring. Under the action of uridine phosphorylase, 5-fluorouracil (FU) is released. DFUR is thus acting probably as a prodrug. DFUR is active against several experimental animal tumors. Further, it has a higher therapeutic index compared to FU in animals. DFUR has been administered as a rapid intravenous bolus injection daily x 5 and repeated every 3 weeks. 21 patients were treated at various dose levels. The majority of patients were non pre-treated and had gastro-intestinal adenocarcinoma or non small cell lung cancer. 2 courses of DFUR or more were administered to 15 patients. A minimum of 4 patients were entered at each dose level. Doses were escalated from 300 - 3000 mg/m²/day. Intra-patient dose escalation was not done. No significant leucopenia was detected, but occasional thrombopenia was seen at each dose level. There was no evidence of cumulative myelotoxicity on subsequent courses of DFUR. Anorexia and nausea was seen in 4 patients, without drug induced vomiting. 2 patients had discrete and 1 patient severe diffuse stomatitis. Precordial pain with reversible electrocardiographic changes or transient cardiac enzymatic elevations was observed in 2 patients. The maximal tolerated dose has not yet been reached. Pharmacokinetic data are available for 5 patients after administration of 1000 to 2100 mg of DFUR. The unchanged drug elimination has a mean t_{1/2} α of 5.6 min. (range 3 - 8.3 min.) and a mean t_{1/2} β of 20.5 min. (range 14.5 to 30.8 min.). Distribution volume β is between 27 and 50 liters. Total plasmatic clearance lies between 0.8 and 1.8 liter/min. We conclude that DFUR can be given at higher doses than FU and that its clinical tolerance is good, at the dose levels tested.

PHASE I TRIAL OF α 1,3,5-TRIGLYCIDYL-S-TRIAZENETRIONE (TGT, NSC-296934)

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TGT is a new anticancer agent that was identified by random screening. It is a tri-epoxide derivative with alkylating properties. The drug is active against a wide variety of experimental murine tumors including P388 leukemia resistant to cyclophosphamide, intracerebrally implanted L1210 leukemia and ependymoblastoma. This ongoing phase I trial was designed to determine the maximum tolerated dose (MTD) in adult patient with solid tumors using daily treatments for 5 consecutive days. The therapy course is repeated every 3 weeks. The drug is given iv. bolus. A total of 33 patients have been entered in the trial with a median age of 59 (38 - 73) and a median performance status of 70 (40-90). All have received prior chemotherapy and had recovered from prior drug-induced side-effects. Patients had following tumors : 8 colo-rectal, 8 lung, 6 breast, 4 melanoma, 2 upper-GI, 2 headneck, 2 unknown origin, 1 sarcoma. The trial was initiated at a starting dose of 12 mg/m²/d corresponding to 1/10 LD₁₀ in the mouse. To date, doses have been escalated up to 600 mg/m²/d (= level 13). Dose levels have been occasionally increased within the same patients when no toxicity was encountered in previous courses. So far not clearly dose-related toxic effects have been observed. Toxic manifestations include nausea-vomiting (6 patients), phlebitis (7 patients) and erratic myelo-suppression (5 patients). So far antitumor activity has not been detected. Since the MTD has not yet been clearly reached, the trial as well as pharmacokinetic studies are ongoing.