

Intensified bimonthly cisplatin with bolus 5-fluorouracil, continuous 5-fluorouracil and high-dose leucovorin (LV5FU2) in Patients with advanced gastrointestinal carcinomas: a phase I dose-finding and pharmacokinetic study.

[Bamias A](#), [Syrigos K](#), [Fountzilas G](#), [Tzamakou E](#), [Soulti K](#), [Karavasilis V](#), [Alamanos Y](#), [Christodoulou C](#), [Pavlidis N](#).

Source

Oncology Department, Ioannina University Hospital, Ioannina, Greece. abamias@med.uoa.gr

Abstract

5-fluorouracil (5FU) and cisplatin are commonly used in the treatment of gastric cancer. Continuous 5FU appears to be more effective and less toxic than bolus administration, while increasing the dose intensity of cisplatin may be advantageous. We conducted a phase I study to establish the maximum tolerated dose (MTD) of cisplatin, which could be combined with a hybrid bolus/continuous 5-FU regimen (LV5FU2), given every 2 weeks. Thirty-six patients with advanced upper gastrointestinal carcinomas entered the study. Starting cisplatin dose was 40 mg/m² and it was increased by 10 mg/m² in cohorts of 3-6 patients. The pharmacokinetics of 5-fluorouracil in 14 patients were compared with those of 6 patients receiving LV5FU2 alone. All patients received prophylactic granulocyte colony-stimulating factor at cisplatin doses \geq 50 mg/m². MTD was reached at 100 mg/m² of cisplatin and, therefore, the 90 mg/m² dose is recommended for phase II studies. Bone marrow toxicity was the most frequent dose-limiting toxicity with 1 patient dying of neutropenic sepsis. Grade III/IV neutropenia was observed in 10 patients (27.7%). Nonhematological toxicity was infrequent and mild. Pharmacokinetic analysis showed that the addition of 90 mg/m² or 100 mg/m² of cisplatin to LV5FU2 significantly reduced the 5FU area under the curve. Objective response rate in 23 evaluable patients was 39.2%. The combination of LV5FU2 with bimonthly 90 mg/m² cisplatin is feasible and active and should be further evaluated in patients with advanced gastric cancer.