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A phase II study with CPT-11 plus leucovorin and bolus IV 5-fluorouracil in patients with advanced colorectal carcinoma.

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Source

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Abstract

Standard chemotherapy in advanced colorectal carcinoma (CRC) has not yet been established. The present study was conducted to assess the efficacy and toxicity profile of CPT-11, leucovorin (LV), and bolus 5-fluorouracil (5-FU) in a weekly schedule. Fifty-five patients were entered with no prior chemotherapy for advanced disease or adjuvant treatment ended at least 6 months preceding study entry, and 45 were assessable for response. Patients were treated with CPT-11 80 mg/m2 (7 patients) or 70 mg/m2 (48 patients). After completion of CPT-11 infusion, LV 200 mg/m2 was administered over 2 hr followed immediately by 5-FU 450 mg/m2, IV bolus, weekly for 6 weeks followed by a 2-week rest period. Treatment was continued for four cycles. Because of grade 3 and 4 diarrhea in four of the first seven patients, the study was amended to reduce the starting dose of CPT-11 from 80 to 70 mg/m2 weekly. Four complete and 10 partial responses were observed (response rate: 25.5%), the median time to progression (TTP) was 7.7 months, 1-year survival rate was 62.3%, and the median overall survival was 15.0 months. Grade 3 and 4 diarrhea occurred in seven patients (12.7%), four of them treated with CPT-11 80 mg/m2. Grade 3 myelotoxicity occurred in five patients (9.0%). Toxic death because of diarrhea, neutropenia, bacteremia, and sepsis occurred in a patient treated with CPT-11 80 mg/m2. Our results confirm the efficacy of CPT-11, LV, and 5-FU in a weekly schedule in patients with advanced CRC. Further studies are needed to compare the present regimen with higher doses of CPT-11 with LV plus different schedules of 5-FU administration in the treatment of metastatic CRC.