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Second-line chemotherapy with weekly oxaliplatin and high-dose 5-fluorouracil with folinic acid in metastatic colorectal carcinoma: a Hellenic Cooperative Oncology Group (HeCOG) phase II feasibility study.

Janinis J, Papakostas P, Samelis G, Skarlos D, Papagianopoulos P, Fountzilas G.

Source

Third Department of Clinical Oncology, St. Anargiri Cancer Center, Athens, Greece. hecogoff@otenet.gr

Abstract

BACKGROUND:

Oxaliplatin is a novel platinum derivative, which, combined with 5-fluorouracil (5-FU), and folinic acid (FA), demonstrates synergistic activity in metastatic colorectal cancer (MCC). The HeCOG performed a multicenter phase II study of a weekly oxaliplatin administration schedule in patients with previously treated MCC to evaluate the antitumor efficacy and toxicity of this combination.

PATIENTS AND METHODS:

Eligible patients included those who relapsed after or during chemotherapy with 5-FU and FA and/or irinotecan. Prior radiotherapy was accepted provided that measurable disease was outside the radiation fields. Other eligibility criteria included written informed consent, a WHO performance status < or = 2 and adequate bone marrow, liver and renal function. Treatment consisted of Oxaliplatin 50 mg/m2 by two-hour intravenous (i.v.) infusion followed by FA 500 mg/m2 (two-hour i.v. infusion) and 5-FU 2,500 mg/m2 (24-hour continuous i.v. infusion) on days 1, 8, 15, 22, 29, 36. The regimen was repeated every 50 days.

RESULTS:

Thirty-two patients (Median age 61 years, range 25-76) entered the trial. The majority (75%) had progressed after receiving first-line chemotherapy. Diarrhea was the main non-hematologic toxicity. More than half of the patients (53%) developed grades 3 or 4 diarrhea. Due to this side effect only 29% of cycles were given with at least 90% of the planned dose of 5-FU. Hematologic toxicity included grade 3 neutropenia and thrombocytopenia (10% for each), and grade 4 thrombocytopenia (3%). Two patients (6%) died of sepsis, one related to neutropenia and one due to urinary tract sepsis. Sixteen patients (50%) developed grades 1 and 2 neurotoxicity in the form of sensory neuropathy, which was mild and transient. The objective response rate was 13% (95% CI: 3%-29%). All four responses were partial. Twelve patients (38%) had stable disease and 8 (25%) progressive disease. The median time to progression was three months and the median survival was nine months from the start of therapy. The Kaplan-Meier estimated probability of one-year survival for the group as a whole was 32%.

CONCLUSIONS:

The weekly administration of oxaliplatin with 5-FU and FA was associated with considerably less neurotoxicity than other schedules. However, the high percentage of diarrhea suggests that a dose reduction of 5-FU in this regimen may result in better therapeutic synergy.