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Short communication

Combination of dacarbazine, mitomycin C, 5-fluorouracil and vincristine in advanced colorectal cancer

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Summary. *Thirty patients with advanced measurable colorectal cancer received monthly courses of a combination of dacarbazine, mitomycin C, 5-fluorouracil, and vincristine (FIVMit-Or). Four of the patients had received prior chemotherapy. Two patients were not evaluable for response. Objective response was obtained in four patients. Severe toxicity was encountered in 11 patients. It is concluded that unlike the fourdrug combination of 5-fluorouracil, DTIC, vincristine and BCNU (FIVB), the present regimen did not have significant antitumour activity in advanced colorectal cancer.*

Introduction

Encouraging results have been reported in patients with advanced colorectal cancer treated with a combination of dacarbazine and mitomycin C [2]. A recently published study failed to confirm this finding [1]. Response was documented in 43 of 112 patients with advanced colorectal cancer treated with the four-drug combination 5-fluorouracil, dacarbazine, vincristine, and BCNU (FIVB) [3]. The present study investigated the substitution of Mitomycin C in this four-drug combination.

Materials and methods

All patients had measurable lesions of histologically confirmed colorectal carcinoma no longer curable by surgery or radiotherapy. Eligibility criteria included performance status (PS) of 3 or better [4], white blood cell count $\geq 4{,}000/mm^3$, platelets $\geq 100{,}000/mm^3$, serum creatinine ≤ 1.5 mg/100 ml, and bilirubin ≤ 2mg/ml. Full recovery from prior treatment was required. The treatment regimen consisted of 5-fluorouracil 425 mg/m^2 IV on days 1–5, dacarbazine 325 mg/m^2 IV on days 1 and 2, and vincristine 1 mg IV and mitomycin C 10 mg/m^2 IV on day 1. All patients were also given ethyloestrenol 4 mg daily. Treatment courses were repeated at monthly intervals if the haemogram had recovered from the effects of the previous treatment cycle. Treatment was delayed until such recovery occurred. Doses were modified if the nadir white blood cell count was $< 2{,}000/mm^3$ and/or nadir platelet count was $< 75{,}000/mm^3$. The criteria for response were those used by ECOG [4].

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Results

Thirty patients were entered on study. Five of the patients had prior treatment apart from surgery (1 radiotherapy, 1 radiotherapy plus 5-fluorouracil, 1 5-fluorouracil, 1 5-fluorouracil plus hydroxyurea, and 1 chlorozotocin). Two patients were not evaluable for response, refusing treatment after one and two cycles. Of the 30 patients, 11 were men and 19 were women, with a median age of 62 years (range 25–81). Twenty-five patients had colon and five patients had rectum cancer. Twenty-two patients had liver metastases. Performance status (PS) [4] at the start of treatment was: 0 in seven, 1 in nine, 2 in eleven, and 3 in three patients. One patient received 18 courses of treatment, four patients received nine to 15 courses, 10 patients received three to eight courses, and 10 patients received two. Four patients received one course only.

Toxicity

The toxicity is shown in Table 1.

Therapeutic effect

Four of the 28 evaluable patients had a partial response, lasting 82, 58, 32, and 10 weeks. In 18 the disease remained stable for 8–87 weeks. In six patients disease progression occurred within 2 months after starting treatment.

Survival

The median survival time for patients is 23 weeks. Five patients are still alive. The median survival time of patients with PS 0–1 is 32 weeks, while for those with a PS 2–3 it was 21 weeks.

Table 1. Toxicity grade

Toxicity grade[a]	I	II	III	IV
Anaemia	8	2	1	–
Leukopenia	2	2	–	–
Thrombocytopenia	2	–	–	1
Nausea + vomiting	3	8	5	–
Diarrhoea	2	2	2	–
Stomatitis	4	–	1	–
Uraemia	–	2	1	–

[a] ECOG toxicity criteria [4]

Discussion

The response reported to the combination of dacarbazine and mitomycin C [2] led us to substitute mitomycin C for BCNU in the FIVB combination. In the present study a response in four of 28 evaluable patients (14%) indicates a response rate of 4%–32% at the 95%-confidence level, and does not offer promise for further clinical trial. The median survival time of 23 weeks likewise does not show promise. It is therefore concluded that although dacarbazine appears to play a role in the therapeutic effect of the FIVB combination, substitution of mitomycin C for BCNU makes the drug combination less effective.

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