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Fotemustine in Patients with Advanced Gastric Cancer, a Phase II Trial From the EORTC-GITCCG (European Organization for Research and Treatment of Cancer, Gastrointestinal Tract Cancer Cooperative Group)

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Fotemustine activity was evaluated in 26 patients, mostly pretreated, with advanced gastric cancer. Its main toxicity was haematological with grade 3–4 neutropenia in 32% and grade 3–4 thrombocytopenia in 50% of the patients, complicated by 2 toxicity-related deaths due to haemorrhage. No complete or partial responses were observed in the 26 eligible patients and median survival was only 11 weeks. Fotemustine therefore has no activity in advanced gastric cancer. Copyright © 1996 Elsevier Science Ltd

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CT:1; insufficient blood count:2); of the 26 patients, 1 had never been treated. The median number of cycles administered was three (range 0–8) and the dose administered was 100% ± 4% of the scheduled dose for the initial part of the treatment.

Toxicity

Grade 3–4 haematological toxicity was observed in 32% of patients for white blood cells and in 50% for platelets during treatment. We also observed delayed haematological toxicity at weeks 5–7 after discontinuation of chemotherapy in the 12 evaluable patients with more than 35 days of follow-up after start of the treatment. Non-haematological toxicity was low: grade 2 and 3 vomiting in 24 and 16%, respectively, grade 1, 2 and 3 alopecia in 4, 4 and 8%, respectively, and general malaise or flu-like syndrome in 4 patients (16%). Two deaths were due to massive digestive haemorrhage from the tumour which was certainly related to grade 4 thrombocytopenia.

Responses

With WHO criteria, no objective responses were observed, but 4 patients had disease stabilisation for more than 4 weeks. In contrast, disease in 5 patients progressed very rapidly, and 1 died of tumour progression even before administration of fotemustine and another after the first cycle. Treatment was discontinued due to tumour progression in 70% of the cases and because of toxicity in 8%. Treatment was interrupted in 1 patient because of pulmonary embolism. 1 patient was lost to follow-up.

Survival was short with a median of 11 weeks and a range of 10 days to 37+ weeks.

DISCUSSION

Fotemustine exhibited no activity on advanced gastric cancer in this study, although most of the patients were, apparently, in good general condition. This may be related to the fact that all but 1 of the patients had been pretreated, thus emphasising how difficult it is to assess a new drug’s activity for gastric cancer in a second-line setting; disease will progress in many patients very rapidly even before planned treatment, as was the case in 1 of our patients. Indeed, only 14/26 received 3 or more cycles of chemotherapy and only 1 received the full course of treatment (8 cycles). With no response in 14 patients, activity must be excluded in more than 15% of pretreated patients.

One of the reasons for such a lack of efficacy could be the schedule used in this study. The 5-week rest period after induction treatment could promote tumour progression in these rapidly growing tumours. It is noteworthy that one of the most efficient chemotherapy protocols, the FAMTX protocol, administers chemotherapy every 2 weeks [6]. Thus, it cannot be excluded that another mode of administration (i.e. every 3 weeks) or combination with a non-haematotoxic drug could lead to activity in AGC, although previous trials using combination 5-FU and methyl-CCNU, another nitrosourea, yielded no significant activity [7, 8].

Although the true activity of fotemustine in untreated gastric cancer has yet to be demonstrated, fotemustine with this schedule has clearly not improved our therapeutic armamentarium in advanced gastric cancer. These results are unfortunately very similar to those observed with fotemustine and the same protocol in advanced colorectal cancer [9].


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