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Clinical Trial Summary

A Phase II Trial of Continuous Infusion Vinblastine in Patients with Gastric Carcinoma

A Southwest Oncology Group Study

DANIEL D. VON HOFF,* PHYLIS J. GOODMAN,† CARY A. PRESANT,‡ ROBERT L. RUXER,§ JOHN S. MACDONALD,‖ JOHN J. COSTANZI,¶ RONALD L. STEPHENS** and STANLEY J. VOGEL**

**University of Texas Health Science Center, 7703 Floyd Curl Drive, San Antonio, TX 78284-7884, †Southwest Oncology Group Statistical Center, Seattle, WA, ‡The Central Los Angeles CCOP, §Wilford Hall Medical Center, San Antonio, TX, ‖University of Kentucky Medical Center, Lexington, KY, ¶University of Texas Medical Branch—Galveston, Galveston, TX and **University of Kansas Medical Center, Kansas City, KS, U.S.A.*

INTRODUCTION

ALTHOUGH there are several combination chemotherapy regimens which have been developed to treat patients with advanced gastric cancer there is still clearly a need for new agents with activity against the disease. Vinblastine is an old agent which has had only limited phase II testing in patients with advanced gastric cancer. Comis and Carter reported cumulative data from four small studies showing three objective partial responses in a total of 16 evaluable patients [1]. Al-Sarraf *et al.* observed four partial responses in 11 evaluable patients treated with the combination of vinblastine and 5-fluorouracil [2]. Inaba *et al.* noted vinblastine was one of the most active chemotherapeutic agents against human gastric tumors growing in nude mice with a 30% overall response rate [3]. Based on the responses noted in the above clinical trials as well as the nude mouse data, it was felt another trial to determine the single agent activity of vinblastine in patients with advanced gastric cancer was warranted.

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Address correspondence to Daniel D. Von Hoff, M.D., F.A.C.P., University of Texas Health Science Center, MED/Oncology, 7703 Floyd Curl Drive, San Antonio, TX 78284-7884, U.S.A.
Address reprint requests to Southwest Oncology Group (SWOG 8235), Operations Office, 5430 Fredericksburg Road, Suite 618, San Antonio, TX 78229, U.S.A.
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PATIENTS AND METHODS

Patients with advanced measurable gastric carcinoma with or without prior chemotherapy were eligible for this study. Patients were classified on the basis of prior chemotherapy. Patients had to have an absolute granulocyte count $\geq 2000/\mu l$, a serum creatinine <2.0 mg/dl, serum bilirubin <2.0 mg/dl, and a performance status of 0–3.

TREATMENT

The initial dose of vinblastine sulfate was 1.4 mg/m^2 by a continuous infusion through a central venous catheter for 5 days. The infusion was repeated every 3 weeks provided the absolute granulocyte count was $\geq 1500/\mu l$ and the platelet count was $\geq 100{,}000/\mu l$. Dose escalations (15%) were performed if nadir granulocyte counts were $\geq 1500/\mu l$ and nadir platelets counts were $\geq 100{,}000/\mu l$.

RESULTS

Fifty patients were entered on this study by 19 institutions. Three patients were found to be ineligible because they did not have measurable disease. There were 18 eligible and evaluable patients who had received prior chemotherapy and 29 evaluable patients who had not received prior chemotherapy (see Table 1).

Table 1. Patient characteristics and responses

Parameter	Total	Prior chemotherapy	No prior chemotherapy
Evaluable for response and toxicity	47	18	29
Male/Female	31/16	8/10	23/6
Median age (range)	64.0 (36–81)	60.5 (36–79)	66.0 (48–81)
Previous treatment			
None		0	29
Radiotherapy		3	0
Chemotherapy		18	0
FAM		14	0
5FU		2	0
5FU + CCNU		1	0
5FU + DDP		1	0
Performance status			
0		2	5
1		8	13
2		5	7
3		3	4
Response			
Partial response	1	1	0
Stable disease	7	1	6
Increasing disease	26	12	14
Early death — assumed no response	10	2	8
No evaluation performed — assumed no response	3	2	1

Ten patients died prior to the first disease assessment and three patients were removed from treatment either due to toxicity (one patient) or refused further therapy prior to the first disease assessment (two patients). For these 13 patients we have assumed no response.

There was one partial response (standard Southwest Oncology Group criteria) in a patient who had received prior chemotherapy (5FU + CCNU). The response began 3 months after treatment started and lasted 2 months. No partial or complete responses were noted in the 29 patients with no prior chemotherapy. A total of 29 patients were entered because in the first 14 patients we had noted two hints of antitumor activity (less than partial responses). However, these hints of activity were not confirmed in the subsequent 15 patients entered.

The response rate in the group of patients who received no prior chemotherapy is 0% (0/29) with a 95% exact confidence interval of 0–11.9%, and the response rate in the group who received prior chemotherapy is 6% (1/18) with a 95% exact confidence of 0.1–27.3%. All but one of the patients have died. The overall median survival is 3.8 months.

All 47 patients were evaluable for toxicity. There were two possible treatment-related deaths. One patient died of sepsis due to neutropenia. The second patient died of an acute pulmonary embolism 12 h after chemotherapy. This death was questionably due to the drug. Three patients had grade 4 (SWOG criteria) life-threatening toxicity. Two of them had granulocytopenia and one had ileus/constipation. Thirty-eight per cent of patients had some hematologic toxicity. In addition to the patient with the death due to the acute pulmonary embolism 12 h after chemotherapy there were two other patients who died of pulmonary embolism. Neither of these episodes were felt to be drug related.

DISCUSSION

We have not been able to document any other previous large standard single agent phase II studies of vinblastine in patients with gastric carcinoma. In particular, the efficacy of continuous infusion vinblastine against advanced gastric carcinoma has not been previously studied.

Unfortunately, in the present study continuous infusion vinblastine does not appear to be an active agent in patients with advanced gastric carcinoma despite administration of a biologically active (myelosuppressive) dose of the agent.

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