A Clinical Trial Adriamycin (NSC 123127) in Advanced Sarcomas

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Key Words

Adriamycin
Sarcomas

Abstract

22 patients with advanced sarcomas received adriamycin, 20–25 mg/m²/day for three days each three weeks. Two patients manifested objective response for a median of five months. Eight patients had stable disease for a median of three months. Nausea and vomiting occurred in 21 of 22 patients; leukopenia in eleven of 22; thrombocytopenia in four of 22. There was no clinically significant cardiotoxicity. Our study indicates that this regimen for adriamycin was relatively ineffective in the management of these inoperable or metastatic malignancies.

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Introduction

Single agent chemotherapy with adriamycin in advanced sarcomas has produced response rates of 10–40 % [1]. Dose schedules have included ranges of 60–105 mg/m² as a single dose every three weeks, or 20–30 mg/m² for three days every three weeks. The various programs seem to have the same effectiveness for bone and soft tissue sarcomas [2]. This report summarizes our experience with adriamycin in patients with inoperable or metastatic sarcomas of bone and soft tissue.

Materials and Methods

The 22 patients with a mean age of 38 years were entered on study from December, 1971, through September, 1972. All patients had visceral-dominant disease and only seven had prior chemotherapy. The 22 patients were acceptable candidates for cytotoxic therapy relative to hematologic status and performance score.

Adriamycin was given intravenously at a dose of 20–25 mg/m²/day for three days every three weeks for two courses. Patients with objective evidence of tumor regression after two courses were randomized between a three-day course of therapy on four- or six-week intervals. Patients with objective progression of disease were dropped from study, but follow-up was continued. A partial regression was defined as a = 50 % decrease in the product of diameters of measurable lesions for a minimum of four weeks. A complete regression was defined as the disappearance of all evidence of disease. Progressive disease was defined as the appearance of any new lesions, or an increase in the previous lesions by > 25 %.

Results

Two of 22 patients showed objective regression for duration: of four and six months; eight of 22 patients had stable diseases < for a median of three months (table I). Three of eight patient;

remaining stable had hemangiopericytomas. However, small numbers precluded meaningful comparison by cell type. Five patients each were randomized to four- or six-week treatment schedules; there was no difference in the number of patients remaining stable or responding. The ten patients remaining either stable or responding lived a median time of ten months after starting chemotherapy; the twelve non-responders lived a median of five months after initiation of chemotherapy. Nausea, vomiting, and alopecia occurred in 95 % of patients, but stomatitis in only one patient. Leukopenia (WBC < 3,000/mm³) was noted in eleven of 22 patients, but thrombocytopenia was rare. There was no clinically significant cardiotoxicity.

Discussion

Our patients had generally good performance scores, were relatively young, and had no substantial non-malignant con-

Table I. Responses by diagnosis.

Cell Type No. of Objec- Duration Objec- Duration patients tive re- (months) tively (months)
sponses stable
(> 3 months)

Osteogenic

sarcoma	7	14	0	0		
Leiomyosarcoma	4	16	13	Hemangiopericytoma	3 0 0 3	3,3,4Lipomyxo-
sarcoma	2	0	0	0	0	
Rhabdomyosarcoma	2	0	0	2	3,4	Synovial cell
sarcoma	2	0	0	15		
Fibrosarcoma	2	0	0	18		

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ditions. Nevertheless, this report showed a disappointing response to adriamycin, a finding consistent with another study of sarcomas treated with a comparable dose of adriamycin [3]. On the other hand, some reports note responses of 33–40 % with adriamycin given as a single dose of 60–75 mg/m² each three weeks [4, 5]. Gastrointestinal and hematopoietic toxicities were less frequent with the single high-dose schedule than in our study. Current data indicate that the antitumor activity of adriamycin is dose-dependent and may be more effective in patients with minimal residual disease rather than with large tumor burdens as in our study [6].

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Cortes

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