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Clinical Trial Summary

Phase II Multicentre Study of the Nitrosourea Fotemustine in Inoperable Squamous Cell Lung Carcinoma

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INTRODUCTION

FOTEMUSTINE is a new amino acid phosphonate derivative of the nitrosourea group which has yielded good response rates in disseminated malignant melanoma (24.2%). It is associated with a good tolerance and an improved survival time [1, 2]. Other phase II studies have conducted investigations in other tumor types [3, 4]. The present study concerns the results obtained in squamous cell lung cancer.

MATERIALS AND METHODS

Between January 1986 and October 1988, 40 evaluable patients with inoperable squamous cell carcinoma of the lung received fotemustine whatever the prior treatment administered. Five French centers entered five patients or more. Eligibility criteria included: Karnofsky scale >60%, white cells >4000/mm^3, granulocyte count >2000/mm^3, platelets >150,000/mm^3, serum creatinine <150 μmol/l and evidence of evolution in disease during the two preceding months. Patient characteristics are shown in Table 1.

Prior chemotherapy, even including nitrosourea, was not among the exclusion criteria. Three cases of previous CCNU treatment were found among the 17 patients (43%) who had had prior chemotherapeutic treatment. Only 14 patients had never received treatment of any sort.

Table 1. Patient characteristics

Evaluable patients	40
Male:female	37:3
Median age	50 (41–75)
UICC classification	
stage III	14
stage IV	26
Median performance status	90 (70–100)
No prior chemotherapy	23 (57%)
surgery	4
radiotherapy	3
surgery and radiotherapy	2
no prior treatment	14
Prior chemotherapy	17 (43%)
and radiotherapy	8
and surgery	1
alone	8
prior treatment with nitrosourea (CCNU)	3 (7%)
Metastatic sites	
lung	38
central nervous system	10
bone	7
liver	6
lymph nodes	4
adrenal gland	2
Responders	5
stage III	
— prior chemotherapy	1
— prior radiotherapy and chemotherapy (including CCNU in one)	2
stage IV	
— no prior chemotherapy or radiotherapy	1
— prior chemotherapy	1

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All patients were administered 100 mg/m^2 of fotemustine on days 1, 8 and 15, followed by a 5-week rest period. The drug was dissolved in 250 cc of 5% glucose solution and administered as an i.v. infusion over 1 h, and special precautions were taken to avoid its contact with light.

Maintenance therapy in responding or stabilized patients consisted of 100 mg/m^2 once every 3 weeks, depending on hematological status. Hospitalization was not necessary during administration of treatment.

Response and toxicity were evaluated according to the WHO criteria [5].

RESULTS

Partial response (PR) was achieved in five patients (12.5%, with 95% confidence interval 2–22%). No change (ST) was observed in 12 patients (30%) and progression in 23 patients. All responses were observed on lung targets.

It is noteworthy that among the PR, four of the five patients received prior treatment (one or two regimens) including one patient pretreated by a nitrosourea.

Median duration of response was 28 weeks for PR (range 26–59 weeks) and 16 weeks (10–25) for ST. Median duration of survival was 43 weeks in patients achieving response or stabilization, and 16 weeks for patients with progressive disease.

The main toxicity was hematological, characterized by delayed but reversible leucopenia (grade IV: 20%, nadir: day 43) and thrombopenia (grade IV: 29%, nadir: day 35). Eleven patients (31%) presented a transient and reversible increase in hepatic biologic parameters. Nausea and vomiting were very mild (80% of grades 0 and I). No other toxicity was encountered, especially no alopecia.

CONCLUSION

Despite hematotoxicity found in our study, the observed response rate (12.5%), particularly in pretreated patients, the median duration of response (28 weeks), the median duration of survival (43 weeks) and the good clinical tolerance are promising results.

Less hematotoxic schedules have been reported: fotemustine 100 mg/m^2 day 1 and day 8 [2] and a controlled trial using combination regimen, based on this schedule, is ongoing.

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