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Clinical Trials Summaries

Phase II Study of High Dose Ifosfamide Plus Mesna in Inoperable Non Small Cell Lung Carcinoma

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IFOSFAMIDE is an alkylating oxazaphosphorine analog of cyclophosphamide which has been reported to give a 32–39% response rate in non small cell lung carcinoma (NSCLC) [1, 2].

This high degree of activity was not confirmed by more recent studies [3], but the adjunction of mesna avoiding bladder toxicity led us to test high doses of Ifosfamide looking for a dose effect [4].

MATERIALS AND METHODS

Between April 1985 and July 1986, 30 patients with inoperable NSCLC received Ifosfamide plus mesna as first line chemotherapy treatment.

Eligibility criteria included performance status (Karnofsky scale) greater than 50%, objectively measurable disease, granulocyte count $> 2000/mm^3$, serum creatinine < 120 μmol/l and informed consent. Characteristics of the patients are shown in Table 1.

All patients received 4 g/m^2/day of Ifosfamide on 2 consecutive days with mesna 8 g/m^2 over 48 h every 4 weeks. Ifosfamide was dissolved in 2000 ml of 5% dextrose saline solution and administered as an i.v. infusion over 12 h by day and mesna was given as 24 h continuous infusion.

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

Table 1. Patient characteristics

Patients	30
Male:female	27:3
Age	
35–79, median 55 years	
Histological type	
Squamous cell carcinoma	12
Large cell carcinoma	11
Adenocarcinoma	7
UICC classification	
Stage III	3
Stage IV	27
Performance status	
60–100%, median 90%	
Metastatic sites	
Bone	8
Liver	7
Lymph nodes	6
Adrenal gland	3
Subcutaneous	3
Lung	2
Pleura	2
Spleen	1
Pancreas	1

RESULTS

Of the 30 patients, five received one cycle, nine received two cycles and 16 more than two cycles.

Partial response (PR) was achieved in three patients (10% with a 95% confidence interval of

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2–27%). No change was observed in 13 patients (43%) and progression in 14 patients.

Of the three responding patients, two had large cell carcinoma and one squamous cell carcinoma. All of them had disseminated disease at time of inclusion. Time to tumor progression was respectively 2, 3 and 8 months for the three responding patients. Mean time to progression in the no change group was 3.6 months (range 2–6).

Alopecia was observed in all patients (4 Grade IV and 26 Grade III) and vomiting in 60% of patients despite prophylactic treatment.

Hematological toxicity was seen in two patients (Grade IV in one) and CNS toxicity occurred in one patient.

CONCLUSION

The tolerance of a 8 g/m^2 schedule on 2 days was acceptable in terms of hematological and visceral toxicity but the 10% objective response rate was disappointing and did not incite us to incorporate Ifosfamide in combined chemotherapy regimens for NSCLC.

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