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Clinical Trial Summary

Phase II Study of Pirarubicin in Advanced Non-small Cell Lung Cancer

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PIRARUBICIN is 4′-*O*-tetrahydropyranyl-adriamycin (THP-Adriamycin®), an hemisynthetic analog of doxorubicin [1] which has shown a broad antitumor activity similar to that of doxorubicin [1–3]. Its expected lower cardiotoxicity [4, 5] is potentially valuable in view of future treatment schedules combining chemotherapy and radiotherapy. This led us to test this drug in advanced non-small cell lung cancer (NSCLC).

MATERIALS AND METHODS

From January 1987 to March 1988, 30 patients with advanced NSCLC were entered in our study of pirarubicin as a first line chemotherapy treatment. All patients fulfilled the following eligibility criteria: measurable disease, performance status (Karnofsky scale) greater or equal to 60%, granulocyte count >2000/mm^3, platelet count >120,000/mm^3, serum creatinine <120 μmol/l and informed consent. The characteristics of the patients are summarized in Table 1.

Pirarubicin was administered on 3 consecutive days every 3 weeks at a dose of 20 mg/m^2/day i.v. bolus as previously recommended [5, 6]. Response and toxicity were scored according to WHO criteria [7].

RESULTS

Patients received a mean number of 4.5 courses of pirarubicin ranging from 1 to 13 courses and representing a mean total dose of 272 mg/m^2. Two patients received much more pirarubicin, respectively 748 and 803 mg/m^2.

One patient died early on day 15 of the first course of chemotherapy without any side-effect which might be related to a toxic death.

Partial response (PR) was observed in four patients (13.3% with a 95% confidence interval ranging from 3.8 to 30.7%). Time to tumor progression for these responding patients was respectively 5, 5, 7 and 9 months with an overall survival of 10.5, 11+, 12 and 17+ months from the start of chemotherapy. All of them were stage IV at time of inclusion; three

Table 1. Patient characteristics

Patients	30
Male:female	24:6
Median age	54 years (32–70)
Median performance status	90% (60–100)
Histological type	
Adenocarcinoma	17
Large cell carcinoma	8
Squamous cell carcinoma	5
UICC classification	
Stage III	9
Stage IV	21*
Involved sites in responding patients/all	
Lung	3/27
Liver	2/2
Adrenal gland	1/4
Bone	1/8
Other	0/17
Total	7/58

*Including three patients previously treated by surgery and one by radiotherapy.

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out of four had large cell carcinoma and the fourth had squamous cell carcinoma.

In the 'no change' group, which included two patients with a minor response and 11 with stabilization, the mean time to progression was 6.6 months (range 1.5–13) with a mean survival of 11.5+ months (range 2–23 months).

Alopecia and vomiting were always mild when they occurred. Severe neutropenia occurred in eight patients (grade IV in 3) and only one episode of thrombopenia grade III was seen.

No clinical cardiac toxicity was observed even in the two patients receiving more than 550 mg/m^2 Pirarubicin. However we noticed a significant decline in the isotopic left ventricular ejection fraction, to below 50% in two cases at cumulative doses of 209 and 222 mg/m^2.

CONCLUSION

Pirarubicin 20 mg/m^2/day in a 3-consecutive-day schedule provides a 13.3% objective response rate with acceptable toxicity. Myocardial tolerance should be useful in combination chemotherapy–radiotherapy regimens for NSCLC.

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