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Clinical Trials Summaries

Phase II Trial of Mitoxantrone in Patients with Hepatocellular Carcinoma

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MITOXANTRONE is a synthetic anthraquinone, with a broad spectrum of activity against human tumor cell lines [1]. The clinical trials of this drug showed promising results for hepatocellular carcinoma (HCC) [2–4]. Therefore, we examined the effects of mitoxantrone in patients with unresectable HCC.

The inclusion criteria for the study were patients with HCC demonstrated by angiography, echography and computed tomography. Patient characteristics are shown in Table 1.

Mitoxantrone was administered intravenously at a dosage of 10 mg/m^2 every 21 days. Evaluation of tumor response was performed every 4 weeks. If there were signs of a response, the treatment was continued for as long as possible.

Of the 25 patients who entered into the study, the response could not be evaluated in three patients: two withdrew early from the study due to drug toxicity, and the other patient had to stop the treatment due to an unrelated complication of ischemic colitis. Two of 22 patients showed partial response. The response rate was 9% with a range of 2.9–21.1% within 95% confidence limits. The first sign of response appeared soon after the start of mitoxantrone administration. In one case, the multiple metastatic nodules in the lung disappeared within 4 weeks, with a decrease in the serum AFP level from 199,000 to 5414 ng/ml. In the other patient, the regression of liver tumor and the decrease of serum AFP level to normal were observed 28 days after the beginning of chemotherapy.

Table 1. Patient characteristics and response

Total entered: male/female	20/5 (15)*
Age median (range)	61 (49–78)
Prior chemotherapy: yes/no	7/18
Performance status	
0	5
1	14
2	4
3	2
HBsAg† positive	2
Liver cirrhosis	16
Serum bilirubin mg/dl	1.1 ± 0.7‡
(range)	(0.3–2.6)
Leukocyte × 10^3/μl	5.2 ± 2.4‡
(range)	(2.5–12.4)
Hemoglobin g/dl	12.9 ± 1.2‡
(range)	(11.5–15.1)
Platelets × 10^4/μl	17.0 ± 11.9‡
(range)	(5.5–56.2)
Evaluable for response	22
Partial response	2
Response rate	9%

*Number in parentheses is patients with histology.
†HBsAg: hepatitis B surface antigen.
‡Mean ± S.D.

Toxicity was examined in 24 patients. Grade 1–2 leukopenia was observed in 10 patients (42%) and grade 3 in 14 (58%). Thrombocytopenia occurred in 14 patients (24%), five of them showing grade 3–4. However, all patients tolerated the treatment and recovered after about 4 weeks. Other adverse effects were anorexia (5 cases), nau-

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sea (2) and diarrhea (1), which were mild. A transient increase of serum aminotransferase was observed in nine patients (38%). No patient showed cardiotoxicity.

The clinical value of mitoxantrone for HCC appears to be limited. However, further study is needed to clarify the effects of mitoxantrone in patients with HCC, because the upper 95% confidence limit of the response rate was 21.1%, and there is no active drug for HCC [5].

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