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Short communication

Combination chemotherapy of advanced renal cell cancer with CCNU and vinblastine

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Summary. *No remission was achieved in 15 evaluable patients with measurable metastatic renal cancer treated with CCNU 120 mg/m² (day 1) and vinblastine 0.1 mg/kg body weight (days 1 and 8) repeated every 6th week. Two additional patients were not evaluable for response owing to early death from progressive disease.*

Previously reported beneficial response rates in metastatic renal cancer after treatment with CCNU and vinblastine could not be confirmed.

Introduction

In 1978 Davis and Manalo [1] reported a 24% response rate to combination chemotherapy with CCNU and vinblastine in patients with metastatic renal cell carcinoma (RCC). These promising results led to a phase-II study with the above drugs in 17 patients admitted to The Norwegian Radium Hospital for advanced renal cell carcinoma from March 1980 to July 1982.

Materials

All patients had measurable disease. Nephrectomy had been performed in 16 of them; seven patients had previously received medroxyprogesterone acetate and five patients, other cytostatic drugs. All antitumor treatment was discontinued at least 4 weeks before the trial with CCNU and vinblastine.

Chemotherapy consisted in CCNU 120 mg/m² PO on day 1 and vinblastine 0.1 mg/kg IV on days 1 and 8. Patients without progression after the first cycle could, at the discretion of the investigator, be treated with subsequent similar chemotherapy cycles starting on day 43.

Patients were evaluable for response if they had received at least one treatment cycle. The WHO criteria for response were used [6]. Early death was defined as death within 3 weeks after the start of treatment.

Results

Two patients died of progressive disease before response evaluation (early death).

No remissions were observed among the remaining 15 patients: Eight had progressive disease after one treatment cycle. 'No change' was observed in seven patients, six of whom had progressive disease within the last 2 months before the trial.

No life-threatening side-effects were observed. The nadir platelet count was $35-100 \times 10^9$/l and the nadir white blood cell count, $0.5-5.0 \times 10^9$/l.

Discussion

This report does not confirm the promising results of Davis and Manalo [1]. Our experience with CCNU combined with vinblastine in RCC supports the conclusions of Hahn et al. [5]. These authors did not find significant antitumor activity of the above drug combination in 60 patients with advanced RCC.

It might be argued that the achievement of no change in previously progressing disease should be considered a response to treatment. We do not agree with this opinion. In general, the biological behavior of metastatic RCC is poorly understood. Considerable changes in the natural history of the disease are sometimes observed in an individual patient, even without any treatment. Periods of progression may spontaneously alternate with intervals of stable disease and even spontaneous regression [3].

Furthermore, it might be claimed that response evaluation after only one treatment cycle is inadequate and that, in general, at least two treatment cycles have to be given before the response of chemotherapy can be assessed. With nitrosourea derivatives it is not unusual, however, to evaluate the tumour response 6 weeks after the start of treatment [2, 4]. In addition, clinical experience with chemotherapy in solid tumors shows that the achievement of objective response after two chemotherapy cycles is extremely rare in patients who have not shown any signs of tumor reduction after the first treatment cycle or who have even progressed. This is also confirmed by the present study, where four patients who had no change after the first cycle did not achieve response after subsequent treatment with CCNU and vinblastine. We therefore consider that the response evaluation in the present study was adequate.

In conclusion, the combination of CCNU and vinblastine is ineffective in metastatic renal cell carcinoma.

References

1. Davis TE, Manalo FB (1978) Combination chemotherapy of advanced renal cell cancer with CCNU and vinblastine. Proc ASCO 19: 316

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2. Decker DA, Samson MJ, Baker LH (1983) PCNU in advanced adenocarcinoma of the ovary: A phase II study. Cancer Treat Rep 67: 511–512
3. Failand DJ (1981) Spontaneous regression of metastases of renal cancer. Cancer 47: 2101–2106
4. Hahn DM, Schimpff SC, Ruckdeschel JC, Wiernik PH (1977) Single-agent therapy for renal cell carcinoma: CCNU, vinblastine, thioTEPA, or bleomycin. Cancer Treat Rep 61: 1585–1587
5. Hahn RG, Colin BB, Davis T (1981) Phase II study of vinblastine-CCNU, triazinate, and dactinomycin in advanced renal cell cancer. Cancer Treat Rep 65: 711–714
6. Miller AB, Hoogstraten B, Staquet M, Winkler A (1981) Reporting results of cancer treatment. Cancer 47: 207–214

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