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Letters

Phase II Study of Oral Ftorafur and Uracil in Patients with Advanced Renal Cell Carcinoma

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ONLY A few cytotoxic and biological agents, alone or in combination, have shown activity in advanced renal cell carcinoma (ARCC). Vinblastine, recombinant interferon-alfa and interleukin-2 are the most effective drugs with an objective response rate which varies from 0 to 30%. Patients who respond to therapy tend to be those with minimal tumour burden (i.e. lung metastases alone) and a good performance status. UFT is a combination of ftorafur [1-(2-tetrahydrofuryl)-5-fluorouracil, FT] and uracil in a molar ratio of 1 : 4. Uracil modulates FT by competing with 5-fluorouracil (5-FU) for dihydrouracil dehydrogenase thus enhancing 5-FU uptake by tumour cells [5–7]. Fluoropyrimidines have been reported to induce a 23% remission rate in patients with ARCC [8]. Moreover, a Japanese clinical study showed an objective activity of 28% in 25 ARCC patients treated with UFT [9]. Based on these findings we started this phase II study.

Selection criteria were: histologically confirmed renal cell carcinoma, measurable and/or evaluable advanced disease, Karnofsky index $\geq$ 60%, no prior treatment with chemotherapy or immunotherapy, no central nervous system metastases, serum creatinine $\leq$ 1.2 mg/dl, bilirubin $\leq$ 2 mg/dl, leucocytes $\geq$ 4000/mm^3 and platelets $\geq$ 100.000/mm^3. Informed consent was obtained in all cases. UFT was continuously administered per os three times per day at a daily dose of 400 mg/m^2, (FT mg) until toxicity could not be decreased by dose adjustment or progressive disease. Complete blood count and blood chemistries were performed on days 1 and 15 and repeated every 28 days. Tumour response was assessed on day 28 and every 2 months thereafter. WHO criteria were followed to evaluate response and toxicity. Only patients completing at least 28 days of treatment were considered evaluable for antitumour activity.

Table 1. Patients' characteristics

No. of patients	16
Fully evaluable	14
Non-evaluable	2
Age years (median, range)	62 (39–61)
Sex (female / male)	5/9
Karnofsky index	70 (60–100)
Prior nephrectomy	7
Site of disease	
Primary/ locoregional	7/4
Liver	2
Lung	7
Osseous	8
Subcutaneous	1
Lymphatic	5
Ocular	1

From February 1989 to February 1992, 16 consecutive patients entered this study. The main patient's characteristics are summarised in Table 1. The 2 patients who died at home on days 18 and 25 of therapy were not evaluable, and 14 patients were evaluable for clinical response and toxicity. No patients responded to treatment, 4 had stable disease and 10 progressed.

Thrombocytopenia, leukopenia, mucositis or alopecia were not reported. Nausea and vomiting grade 1–2 were observed in 50% of patients. 1 patient developed diarrhoea grade 3 and needed a 25% dose reduction, while the remaining patients received all of the programmed treatment. Median time to treatment failure was 67 days (range 60–213) and median overall survival time was 155 days (range 56–793+).

We conclude that continuous administration of UFT at an oral daily dose of 400 mg/m^2 has minor toxicity and no activity in previously untreated patients with metastatic renal cell carcinoma.

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