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RESPONSE IN PATIENTS WITH METASTATIC RENAL CELL CARCINOMA (RCC) DURING THE TREATMENT WITH ALPHA INTERFERON IN COMBINATION WITH 5-FLUOROUCACIL.

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In a prospective controlled pilot study 21 patients with M_1 RCC were evaluated for efficacy in the treatment with recombinant ^{1}interferon alfa-2b in combination with 5-flourouracil (5-FU). The clinical response acc. to WHO criteria has been studied. Beside definite metast. (M_1) the most aligibility factors were a prior nephrectomy and a Karnofsky-index greater or equal 70%. Patients with further malignoma, CNS metastases or with a previous chemo-, cytokine or radiation therapy were excluded from the study.

Interferon alfa-2b was given at a dose of 5 MIU subcutaneously days 1-5 every week for 14 weeks. 5-FU was given at a dose of 500 mg/m² days 1-5 in weeks 2, 6, 10 and 14. Mean Karnofsky performance status fell during the 14 weeks of therapy from 88.7% to 81.1% and the mean body weight from 76.7 kg to 74.2 kg. Side effects and laboratoy investigations showed no unexpected characteristics. Most apparent were the reversible changes of platelets, leukocytes, serum alkaline phosphatase and gamma glutamate transaminase. The therapy was well tolerated.

During the 14 weeks the combination therapy led to objective remissions (complete and partial) in 24% (n=5) of patients and in 33% (n=7) to a stable disease. The site of metastases of the responder was in three cases the lung, in one case the lung in combination with positive lymph nodes, and only in one further case the bone (solitary, thoracic vertebra 9). Three patients with stable disease had lung and four had bone metastases. The site of metastases of the non-responder (43%, n=9) was in five cases the lung and in four cases the bones. Only in the non-responder group have been two RCC related deaths (in week 2 and 26). One of these patients had lung and the other bone metastases.

There is obviously a clear trend for lung and soft tissue metastases to respond to the therapy (4 of 12 = 33%), while bone metastases do not or seem poorly to respond (1 of 9 = 8%). The site of metastases remains the most important prognosticator for response on the therapy with interferon alfa-2b in combination with 5-FU.

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INTERLEUKIN-6 AS ANTITUMOUR AGENT IN RENAL CELL CARCINOMA. Stouthard JML[1], Poorter RL[1], Bakker PJM[1], de Vries EGE[2], de Mulder PHM[3], Goey SH[4], Veenhof CHN[1]. Depts. of Medical Oncology, Academic Medical Center Amsterdam[1], Univ. Hosp. Groningen[2], Univ. Hosp. Nijmegen[3] and Daniel den Hoed Cancer Center Rotterdam[4] the Netherlands.

Recently, a phase II trial investigating the antitumour effects of interleukin-6 (ILS 969, Sandoz, Basel) in patients with metastatic renal cell carcinoma (RCC) with or without previous immunotherapy was initiated. Sofar, 16 patients (pts) entered the study. Five pts (age 65±7 years, no previous immunotherapy) are evaluable for toxicity and response. All pts had measurable and evaluable progressive disease and a performance status (WHO) ≤ 1. Treatment consisted of interleukin-6 (IL-6) 150 µg s.c. once daily for six weeks. Antitumour response was evaluated at week 6 and 10; tolerability and safety were evaluated weekly. Of the 5 pts, one discontinued treatment before week 6 because of rapid progression, and one because of severe mental depression and persistent fatigue. Three pts completed 6 weeks of treatment. One had a ≥ 50 % reduction of liver and pulmonary metastases, one had stable disease and one had progressive disease. All 5 pts experienced gradually subsiding mild rigors and fever after IL-6 injection, not affecting their normal daily habits. Slight weight loss was commonly observed (-2.7±1.9 kg). All showed an increase in platelet count, ESR and CRP, rapidly normalizing after discontinuation of IL-6. An asymptomatic three- to fourfold increase in alkaline phosphatase and gamma-GT was found in two pts, returning towards baseline values once treatment was stopped.

Conclusion: These preliminary results indicate that IL-6 treatment is well tolerated, and may provide a new treatment modality for metastatic RCC.

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ADJUVANT CHEMOTHERAPY OF RENAL CELL CARCINOMA

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Adjuvant chemotherapy of renal cell carcinoma may be reserved to high risk patients (with perirenal infiltration, nodal involvement, bilateral tumors and/or suprarenal metastases, vasal invasion; G3-G4). Material and methods: 36 pat. (24 male, 12 female) after tumornephrectomy, age 42-74 (mean 59,5) years. Chemotherapy consisted of a series of 6 cycles each initiated with CCNU 130 mg/m² p.o. (day 1) + vinblastine 5mg/m² (max.10 mg) i.v. with antiemetic regimen. VBL was continued each 2nd (βrd) week up to 6 doses (= one cycle), the intervals depending upon blood cell counts (WBC, plt). Generally a total of 6 cycles has been aspired with a duration of 1 1/2 - 2 years. Results: 11 pat. (31%) recurrence free survival (observation up to eight yrs), 13 pat. (36%) distant metastases or local recurrence, 12 pat. (33%) death due to cancer. Conclusion: Combination CCNU - vinblastine improves the prognosis of high risk patients with renal cell carcinoma.

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IFOSFAMIDE, VINDESINE AND RECOMBINANT ALPHA-INTERFERONE COMBINATION CHEMOTHERAPY FOR PATIENTS (PTS) WITH PROGRESSIVE METASTATIC RENAL CELL CARCINOMA (RCC).

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Among 49 evaluable pts (34 male; 15 female) with RCC treated between 6/1988 and 9/1992 in our institution by interferone alpha 2b (5 million I.U. s.c. three times weekly on week 2 and 3) in combination with vindesine (3mg/m² on day 1) and ifosfamide (2,5g/m² as 4-hour infusion day 1 to 5 with mesna protection), we have observed an objective (complete and partial) response rate of 24,1% and an overall (complete and partial response and stable disease) response rate of 55,6%. The median duration of remission has not yet been reached, but the survival of responding pts is considerably longer than that of non-responders. Because we could not find any differencies (sex, age, WHO performance status, prior therapy, site of metastatic disease) between responding and non-responding pts, we believe that the treatment might modify intrinsic characteristics of the tumour growth and host-tumour relationship in the long term. Although the toxicity recorded is high, the results are sufficiently positive to justify further investigation of this approach.

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INTERFERON VINBLASTINE AND EPIRUBICIN IN METASTATIC RENAL CANCER

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Metastatic renal cell carcinoma (RCC) is a major therapeutic problem for urological oncologists. Between August 1990 and February 1993, 7 patients with metastatic RCC were treated with a regimen containing alpha-interferon, vinblastine and epirubicin. Toxicity was acceptable with 2 patients requiring treatment delay; there was no chemotherapy related death. Four patients showed partial remission after four cycles of chemotherapy and there was no change in another 2 patients. Four patients progressed of whom 3 died 2,3 and 4 months after treatment, while one patient is still alive with progressive disease 12 months after treatment. This limited data on patients with poor prognostic metastatic RCC warrants further evaluation of this regimen probably with the addition of other biological response modifiers.

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RECOMBINANT INTERLEUKIN-2 (RIL-2) + INTERFERON (IFN) - ALPHA2b IN THE OUTPATIENT CLINIC TREATMENT OF METASTATIC RENAL CELL CARCINOMA (MRC). Santoro A., Maiorino L., Santoro M. Oncology Service, Day Hospital, S.Gennaro Hospital; Naples, Italy.

The prognosis of the MRC is very hard. Till now the chemo and hormonotherapy didn't give reassuring results. For this reason and for the peculiarity of the natural history of the MRC is justified the therapy with biological response modifiers. With the association of IFN - alpha2b and rIL-2 given subcutaneously have been obtained promising results with scarce toxicity, besides have been shown synergic effects with an increase of the therapeutic index. Since April 1991, 6 patients: M/F 5/1; median age 57; 6 pretreated P.S. 0-2 ECOG; have been treated in our institute with the following scheme: rIL-2 9 milion IU/mq was given subcutaneously every 12h days 1 and 2; rIL-2 1.8 milion IU/mq subcutaneously every 12h days 3,4,5,8,10 and rIFN 5 milion IU/mq days 3,5,8,10. This scheme has been continued in alternate days for 6 weeks and repeated every 10 weeks. After 3 cycles we obtained: 1 RP, 3 NC (6+ months), 2 PD. The prominent collateral effects were: fever, asthenia, nausea and hypotension. The reversibility of the toxicity with an adeguate therapy gives practicable this protocol in outpatient basis.