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THE SIGNIFICANCE OF A 21 kDa PROTEIN SERUM LEVELS IN THE FOLLOW-UP OF PATIENTS WITH RENAL CELL CARCINOMA AFTER RADICAL NEPHRECTOMY

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Using an ELISA test, we have previously shown high serum levels of a novel 21 kDa protein (p21) in 78% of patients (pts) with renal cell carcinoma (RCC), as compared with 4.6% of healthy donors. The present study was carried out in order to evaluate the role of serial p21 serum levels in the follow-up of pts with RCC. 19 pts underwent one pre-operative and 1-5 post-operative assays of serum p21, during a follow-up period of 4-18 months. 12 pts showed after surgery a reduction in their initial elevated serum p21 levels, or normal pre- and post-operative levels; they showed no evidence of disease during the follow-up period. 7 pts had persistent high serum p21 levels or an increase in their initial normal p21 levels. At the same time, 3 of them developed distant metastases in lung (2 pts) and in lymph nodes (1 pt). Recurrent disease is being searched in the other 4 pts. In conclusion, post-operative monitoring of serum p21 levels may be used to identify disease progression in RCC, a tumor which doesn't secrete any known marker.

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HIGH DOSES OF NEW ANTIESTROGEN TOREMIFENE IN ADVANCED RENAL CELL CARCINOMA.

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In a pilot phase II stidy 26 pts(20 males,6 females,average age 54,8 years,range 35-73 years) with advanced renal cell carcinoma(relapsed,metastatic) recieved toremifene 300 mg/day p.o. during 2-50 weeks(median - 12,8 w)until progression.Nephrectomy was previously performed in 15 pts.Median size of local tumours was 124,4 cm^2 (range 48-300). In 25 evaluable pts 3 PR(12%) of median duration 8 weeks(range - 3+ to 12 w) and 9 NC(36%) for 6+ to 50 weeks (median - 22 w) were registered independently on lesion site. Total control of severe and moderate pain was achieved in 8 from 14 pts (57%), partial control - in 3 from 14 pts(21%). There were no remarkable side effects, including laboratory tests.There were no cases of early treatment termination because of side effects.It can be suggested that new antiestrogen toremifene in high doses is well tolerated and helpful in palliation of pts with advanced renal cell carcinoma.

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Prognostic factors and survival in patients with metastatic renal cell carcinoma (MRCC) treated with chemotherapy (CHEMO) or Interferon-α (IFN)

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159 pts with MRCC treated with CHEMO (IGR, 1975-90) and 136 pts IFN (NRH, 1983-90) were analysed with regard to prognostic factors. The 3-year survival rate for the CHEMO group was 8% and for the IFN group 25%. In all 295 pts the following parameters were correlated with improved survival: age ≤ 60 years, nephrectomy, time of diagnosis to start of treatment for metastatic disease ≥ 12 months, performance status 0/1 (WHO), absence of liver metastases, ESR ≤ 100mm, weight loss ≤ 10%. In the multi-variate analysis performance status, weight loss and ESR remained independent prognostic factors. These factors separated low-risk and high-risk groups. In the high-risk group there was no survival difference between pts treated with IFN and those receiving CHEMO. CHEMO-pts in the low-group had a 14% 3-year survival. The low-risk IFN-pts displayed a 35% 3-year survival (p=0.02). The survival rate for the IFN-pts was similar to that recently recorded by Palmer et al. (Ann Oncol 3, 475, 1992) for MRCC pts receiving intravenous Interleukin-2.
Conclusion: In MRCC performance status, weight loss and ESR are easily assessable prognostic parameters for the identification of a high-risk and a low-risk group. With all limitations due to the retrospective nature of this study we hypothesize that IFN therapy might be life-prolonging in low-risk pts, but seems to be ineffective in high-risk pts with MRCC.

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RESULTS OF A PHASE-II STUDY OF COMBINATION TREATMENT OF PATIENTS WITH METASTATIC HYPERNEPHROMA WITH RECOMBINANT INTERFERON-ALPHA AND INTERLEUKIN-2

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In a multicenter phase-II study we treated 24 patients with metastatic hypernephroma with a combination of Interleukin-2 (Proleukin, Eurocetus) in a dose of 18 x 10^6 IU/m^2/d continuous i.v. infusion on days 1 to 5 and 8 to 12 and interferon-alpha (Intron-A, Schering Plough) 6 Mio U/m^2 subcutanously on days 1,3,5,8,10 and 12. After a rest period of 2 weeks the treatment was repeated again. Five CR's (23%) and 3 PR's (9%) were observed in 22 patients evaluable for response. Toxicity was managable on a routine medical ward but necessitated dose modification in 68% of the first 2 cycles. The most severe toxicities observed were one case of ischemic colitis followed by perforation and one case of lethal pulmonary emboli. It is remarkable, that some patients remain in unmaintained remissions for now up to 39 months. In the present study combination treatment with interferon-interleukin-2 was found to be an effective, although toxic treatment.

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EVIDENCE FOR A FAVORABLE EFFECT OF SURGICAL RESECTION OF RESIDUAL METASTATIC RENAL CELL CARCINOMA (RCC) FOLLOWING BIOLOGICAL THERAPY (BT).

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We reviewed 31 patients (Pts) with metastatic RCC who underwent resection of residual disease after BT with Interferon-α (25 Pts) or Interleukin-2 based combinations. Responses prior to surgery were: partial response (PR) 22 Pts (71%) minor response (MR) 3 Pts (10%) and stable disease 6 Pts (19%). Surgical sites included: lung (17 Pts), primary tumor (13 Pts), lymph nodes (4 Pts), bone (2 Pts), and liver or omentum (1 Pt). No surgical mortality occurred. Twenty-eight (90%) specimens contained viable disease. Following a median of 11 (3-37) months (mos) after surgery, 15 (48%) Pts remain disease-free. Pts with residual diploid tumors had significantly longer disease-free survival-17.2 vs 8.2 mos for diploid tumors. We conclude: 1. Residual radiographic RCC is very likely to contain viable disease. 2. Surgery for residual RCC is safe and may benefit Pts selected by response to BT (PR, MR) with residual diploid tumors. Prospective studies are needed to confirm the role of residual tumor resection after response or stabilization with BT.

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TAXOTERE (T) IN ADVANCED RENAL CELL CARCINOMA (RCC). A PHASE II TRIAL OF THE EORTC EARLY CLINICAL TRIALS GROUP.

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T (RP 56976, NSC 628503) is a semisynthetic compound. It is an analogue of Taxol with equal or better preclinical activity. Our group has already shown activity of T in second line therapy in breast and ovarian ca. 33 chemotherapy naive pts with metastatic RCC received T, 100 mg/m^2 1h iv every 3 weeks. For evaluation of response at least 2 courses (crs) had to be observed. The trial is closed for entry, 7 pts are still on study. Pts characteristics: median age 63 yrs (range 30-72), median PS 1 (range 0-2). A total of 88 crs (range 1-6) was evaluated. Predominant toxicity (tox) was myelosuppression, especially short lasting granulocytopenia.

tox-grade WHO	anemia pts/crs	leucopenia pts/crs	neutropenia pts/crs	thrombocytopenia pts/crs
1+2	19/35	13/40	7/22	2/3
3	2/3	16/31	9/22	-
4	-	3/3	14/25	-

A wide range of non-hematol tox was observed: nausea, vomiting, hypersensitivity, skin tox, asthenia, diarrhea and progressive edema. Short lasting partial remissions, confirmed by external review, were seen in 2 patients. T has only modest activity in metastatic RCC, myelosuppression is the dose limiting toxicity.