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## Chromophilic renal cell carcinoma: Characterization of four permanent cell lines

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**Purpose:** We are the first to report on the establishment of permanent cell lines, derived from chromophilic renal cell carcinoma (RCC).

**Methods and Results:** Immunocytochemically, all cell lines coex-pressed vimentin and cytokeratins. Karyotypic analysis revealed the numerical aberrations typical for chromophilic RCC, i.e. loss of Y and tri- or tetrasomy 7 and 17. Moreover, all cell lines exhibited a complex pattern of autocrine and paracrine growth regulation: **1.** All cell lines expressed mRNA of TGF-beta type I and II receptors but not type III-R. ELISA analysis demonstrated secretion of inactive TGF-beta$_1$ protein in all cell lines. Exposure to TGF-beta$_1$ resulted in a significant ($p < 0.05$) inhibition of proliferation only in chromphi-2 and -3. **2.** PDGF-AA, PDGF-BB and IGF-1 as well as their corresponding receptors were not present in any cell line. **3.** All cell lines exhibited different levels of FGF-4-receptor whereas aFGF mRNA was not detected. Exposure to aFGF resulted in a significant ($p < 0.05$) stimulation of growth in chromphi-1 and -2.

**Conclusions:** The characteristic morphological and cytogenetic features of chromophilic RCCs are preserved in the cell lines chromphi-1 to -4. Moreover, the heterogeneous expression pattern for various growth factors and their receptors suggests complex mechanisms of autocrine and paracrine growth regulation.

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## Cisplatin, etoposide and bleomycin infusion (PEBI regimen) in good-risk patients with germ cell tumors

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Patients with good-risk germ cell tumors have an approximately 85–95% chance of cure with standard chemotherapy. However, acute and late toxicity may be severe and negatively influence the quality of life. In an attempt to reduce toxicity, we evaluated a new schedule including bleomycin administered as a continuous infusion in patients with low and intermediate volume metastatic disease. Patients were treated as follows: cisplatin, 100 mg/m$^2$ day 4; etoposide, 100 mg/m$^2$ day 1 through 5; bleomycin 15 unit bolus day 1 followed by 30 mg as a continuous infusion for 72 hours, with cycles repeated every 21 days. Between 1992 and 1996, 25 patients entered the study and were assessable for response and side effects. Major patients characteristics were: performance status ECOG 0–1; minimal disease 15, intermediate disease 10; median age, 33 (range 15–50). Twenty-one of 25 patients (84%) achieved a complete remission, 2 patients achieved a partial remission, and 2 patients did not respond to the regimen. At a median follow-up of 24 months, 24/25 patients were alive, 21 (87%) were without evidence of disease and 3 had persistent disease. Grade III/IV side effects included leuko-neutropenia (8 patients), anemia (3 patients), and nausea/vomiting (3 patients). No drug related deaths were observed, and no evidence of pulmonary toxicity was registered. In conclusion, the PEBI regimen is an effective and well tolerated regimen in patients with good-risk germ cell tumors and may be considered as a front-line chemotherapy.

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## Phase II study of interferon gamma (rIFN-G) and vinblastine (VBL) in patients with advanced renal cell carcinoma (RCC)

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**Purpose:** The evaluation of activity and toxicity of combination rIFN-g and VBL in advanced RCC.

**Methods:** Twenty nine patients entered the study and twenty seven were evaluable. Twenty three male and four female with median age 64 (44–74) years, median ECOG performance status I (0–2), without previous chemoimmunotherapy. Eighteen patients had received nephrectomy. The rIFN-g was administered at a dose of 100 mcg subcutaneously three times weekly and VBL was administered at a dose of 0.15 mg/kg I.V. bolus (max. dose 10 mg) every two weeks.

**Results:** The response rate was: CR 2/27 pts, PR 3/27 pts, SD 4/27 pts and PD 18/27 pts. Median survival for responders was 11+ months and for non responders was 5 months. Lung was the commonest site of disease with the highest response rate. The toxicity according to WHO criteria was: Anaemia (G1–G3) 3/27 pts, Neutropenia (G1–G3) 4/27 pts, Neurotoxicity G1 5/27 pts and Flu-like symptoms (G1–G2) 22/27 pts. No toxic deaths.

**Conclusion:** rIFN-g combined with VBL is moderately active with mild toxicity in patients with advanced RCC.

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## Paclitaxel-induced growth supression and morphological alterations in different types of human renal cell carcinoma

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**Purpose:** In clinical trials, the antineoplastic agent paclitaxel has shown promising activity against ovarian and breast cancer, but not yet proved its efficacy against renal cell carcinoma (RCC).

**Methods:** The growth inhibitory effects of paclitaxel (Taxol®) were analyzed by MTT-assay in 34 newly established RCC cell lines of different types (28 clear cell, 4 chromophilic and 2 chromophobe RCCs). Paclitaxel-induced microtubule alterations were visualized by indirect immunofluorescence using anti-alpha-tubulin. The frequency of micronuclei was determined by light microscopy.

**Results:** In 32 out of 34 cell lines a marked dose-dependent ($p < 0.05$) growth inhibition became evident after exposure to paclitaxel. Paclitaxel dissolved in Cremophor EL/ethanol (= Taxol®) proved to be more effective than paclitaxel dissolved in DMSO. In all cell lines, a dose-dependent increase in the frequency of micronuclei could be detected. After paclitaxel treatment, microtubule bundles or irregular coarse meshworks of microtubules were observed in clear cell and chromophobe RCCs, whereas exclusively irregular microtubule meshworks but no microtubule bundles were seen in the chromophilic RCCs.

**Conclusion:** Our study indicates that paclitaxel (Taxol®) significantly inhibits the proliferation of human RCC in vitro, irrespective of the histological type. In chromophilic RCCs, paclitaxel-induced microtubule alterations differed from those observed in clear cell and chromophobe RCCs.

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## Radiotherapy in stage I and II seminoma

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**Purpose:** In seminoma patients, radiotherapy of the paraaortic and pelvic nodes results in excellent survival for stage I and II. In this study we report our results of treatment as well as the acute and late treatment morbidity and a incidence of second cancer.

**Methods:** From 1982 to 1994, 324 pts. were irradiated et the Institute for Oncology and Radiology in Belgrade: 279 in stage I and 45 in stage II of the disease. Med. age was 35 years (22–69). Radiotherapy was delivered by linear accelerator (10 MeV) in all except in 8 pts (they were treated by Cobalt 60 unit). The doses were 30 Gy/18 fr. at midplane for both stages (in the majority of pts.).

**Results:** In 87 pts acute gastrointestinal toxicity was registrated. The med. follow-up was 7 years (range 2–13) and the overall survival rate 98% and 91% for stage I and II, respectively. Relapse occurred in 14 pts. 10 pts were cured by radiotherapy and or chemotherapy; 4 pts died from seminoma. Late sequelae were registrated in 18 pts and second cancer in 5 (2-lung, bladder, 2-opposite testis).

**Conclusion:** Radiotherapy is still a treatment of choice in st. I and II seminoma with high probability for cure and a low rate of late irradiation induced complications and relapses.

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## Testis cancer: Endocrinological disturbancies

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Men with testicular cancer are often not fertile showing disturbances in spermiogram and the sexual hormone levels. The kinetic of the hormone levels following the tumour ablation are evaluated.

Sera of 37 consecutive patients with germ cell tumour (15 SEM and 22 NSGCT) were used from testicular vein blood and peripheral blood at