TGCT. The incidence of 2nd metachronous TGCT in pts with chemotherapy for their 1st TGCT was only 0.8% (5 of 592). 12 additional pts were referred for treatment of their 2nd TGCT. Of the 7 pts with synchronous TGCT (median 31 years) 2 had discordant and 5 concordant histology. 3 died of disease or toxicity and 4 are alive with NED. In 22 pts with metachronous TGCT median age at diagnosis of the 1st TGCT was 25 years; median time to the 2nd TGCT was 7.5 years. 9 pts had concordant (6 nonseminoma, 3 seminoma) and 13 discordant histology (1st TGCT nonseminoma in 11). 19 of 22 pts (86%) presented with stage I at diagnosis of the 2nd TGCT. 21 of 22 pts (95%) are alive with NED (median 52 months); 1 pt died from a late relapse of his 1st TGCT.

Conclusion: The incidence of 2nd TGCT is low, especially in chemotherapy-pretreated pts. As the vast majority of pts carries a good prognosis, routine biopsy of the contralateral testicle cannot be recommended.

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Nuclear accumulation of wildtype p53 protein cannot be related to complex formation with mdm2 in human renal cell carcinoma cell lines

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Purpose: As little attention has been paid so far to alternative mechanisms of p53 inactivation, a comprehensive characterisation of the structure and expression of p53 and mdm2 was performed in 38 newly established human RCC cell lines of different histological types.

Methods: DNA sequence analysis of all p53 exons was done by direct sequencing the PCR-amplified exons. Expression of p53 and mdm2 was assessed by Northern blot and immunocytochemistry. Southern blot was used for analysis of mdm2 amplification.

Results: *1.* p53 mutations could exclusively be identified in clear cell RCCs: "hot spot" mutations of exons 5 to 8 were found in 3 cell lines, whereas three other cell lines exhibited a microdeletion in exon 9, a loss of exons 2 to 11, and a mutation in the non-coding region of exon 1. *2.* p53 mRNA was detected in only 11 cell lines by Northern blot. *3.* Nuclear wildtype p53 protein accumulation was observed in 15 cell lines. *4.* No amplification or overexpression of mdm2 could be demonstrated.

Conclusion: These findings provide evidence that a significant proportion of human RCCs shows nuclear accumulation of wildtype p53 protein without mdm2 amplification or overexpression. Further studies will have to elucidate the functional significance and molecular mechanisms of wildtype p53 accumulation in human RCCs.

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Germ cell tumors (GCT) in men with HIV infection

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Purpose: To evaluate frequency, treatment and outcome of HIV+ men with GCT.

Methods: The records of all patients (pts.) with testicular and extragonadal GCT diagnosed and/or treated at our institution between 1/86 and 1/97 were reviewed and analysed with regard to HIV seropositivity.

Results: 7 out of 229 pts. (224 with testicular, 5 with extragonadal GCT) were HIV+ at the time of tumor diagnosis. 2 pts. turned out to be HIV+ after completion of therapy for a non-seminoma (NSGCT). 2 pts. had seminoma (SGCT) and 5 pts. NSGCT. 1 pt. with bilateral stage I SGCT received adjuvant radiotherapy and was lost to follow-up. The other pt. (stage III SGCT) was treated with 4 courses PEI and remained in CR for 48 months. 1 pt. with stage I NSGCT is free of disease more than 10 years after diagnosis and retroperitoneal lymphadenectomy (RLA). 1 pt. (Stage IIA NSGCT) refused RLA but 4 courses PEB were applied for progressive GCT 31 months later; he is in CR for 29+ months. Intensified platinum-based chemotherapy (ECBC) was applied to 2 pts. with advanced NSGCT. 1 pt. achieved a markernegative PR and relapsed, the other suffered progressive GCT. Both pts. developed AIDS and died. 1 pt. (stage IIB NSGCT) received 2 courses PEB after RLA and remains in CR for 10+ months. Under therapy for GCT CDC-category deteriorated in 3 pts. and did not change in 4 pts.

Conclusion: Oncological therapy based on the patients individual situation is recommended for HIV+ pts. with GCT.

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Bilateral germ cell tumors of the testis (GCTT): Report of two institutions experience

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Purpose: This study is undertaken to evaluate the incidence of bilateral tumors in patients (pts) treated at two different institutions for GCTT.

Methods: The medical records of 815 pts with GCTT [395 Seminoma (S) and 420 non-seminoma (NS)] successfully treated between 1/82 and 12/95 have been reviewed. All pts had been treated for their GCTT according to the stage of disease with standard regimens: 328 irradiation, 421 pts chemotherapy (CT) and 66 surveillance. 374 pts received platinum (P)-based CT, whereas 47 pts some other form of CT. Contralateral biopsy at diagnosis of GCTT was not performed in any of these pts.

Results: The median follow-up of these pts was 9.4 yrs (range 1–13 yrs). 3 pts (0.42%) had bilateral synchronous GCTT (2S, 1S/NS). 16 pts developed metachronous GCTT (1.97%). 14 of 805 pts had a testicular primary site at diagnosis of 1st GCTT, 2 of 7 pts initially had an extragonadal (retroperitoneal) tumor ($p < 0.01$). The median interval between 1st and 2nd GCTT was 45 months (mos) (range 5–242 mos). The tumor in the contralateral testicule occurred more frequently if the 1st tumor was NS ($p < 0.01$). In 5 pts (31.25%) histological differences (S and NS) between 1st and 2nd GCTT were found, whereas in 11 pts (68.75%) occurred the same histology (NS 9, S 2). 2 of 421 pts (1.7%) were treated with CT for the 1st GCTT, whereas 5 of 66 pts (7.6%) were on surveillance ($p < 0.05$). 4 of 328 pts (1.22%) had radiotherapy for the 1st GCTT ($p < 0.01$). The median interval between 1st and 2nd GCTT, according to applied primary treatment, was 49, 54 and 67 mos, respectively. After treatment for the 1st GCTT 13 pts are alive NED after median follow-up of 12 mos (range 25–245 mos).

Conclusion: The incidence of bilateral GCTT in our series is less than expected according to the series assessing contralateral carcinoma in situ at the time the 1st tumor is diagnosed. On the bases of these results it is difficult to recommend contralateral biopsy at diagnosis of GCTT in our population. Although CT and irradiation reduce the development of the 2nd GCTT, the risk apparently is not completely eliminated. pts with primary retroperitoneal GCT need a close and careful follow-up, as they appear to be at increased risk for developing a GCTT.

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Interferon-gamma (IFN-g) and interleukin-2 (IL-2) is a feasible and effective out-patient regimen for advanced renal cell cancer

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We designed a phase II study for pts with advanced RCC to study the feasibility, toxicity, and efficacy of out-patient IFN-g+IL-2.1 cycle consisted of 100 mcg IFN-g sq 3 x/week for 2 wks, 4.5 MIU IL-2 sq for 4 consecutive days for the next 2 wks followed by a 2 wk rest period. At least 3 cycles were given and in the case of response therapy was to be continued until PD. Data of 67 pts (39 m/28 f) with a median age of 60 yrs (range: 44–81) are now available. A median of 3 cycles (r: 1–15) have been applied (median observation time [mot]: 22 mos, r: 7–36) and all patients are eligible for feasibility and toxicity evaluation, and 51 patients for response. 45 pts were trained in self-application of the cytokines. No WHO-grade III/IV toxicity has been documented. Side effects consisted of flu-like syndrome grade I/II in 35 pts (56%) despite prophylactic paracetamol and local erythemas after IL-2 application in 11 pts (18%). Only mild myelotoxicity was observed (leucopenia grade I only and no thrombocytopenia). Anemia grade I/II occurred in 25 pts (40%). Response data of 51 patients (mot: 10 mos, r: 5–16) are: CR:n = 2 (4%), PR:n = 4 (8%), SD:n = 19 (37%), PD: n = 26 (51%). This preliminary data shows that IFN-g/IL-2 is a feasible regimen with acceptable toxicity which can be easily applied on an out-patient basis. The objective remission rate (CR + PR) with 12% and the response rate (CR + PR + SD) of 49% proves the activity of this therapy in RCC. This data are comparable with other cytokine regimens which usually need hospitalization, are more toxic, and are less cost-effective (e.g. infusional IL-2).