pat. one, in further 14 pat. two and in 11 pat. three and more organs were involved. An average of 1.77 cycles was applicated. The systemic side effects corresponded to a toxicity WHO grade 1 in 6 pat., grade 2 in 27 pat. and grade 3 in further 6 pat.

Results: In 6 pat. (15.4%) a complete remission and in 2 pat. (5.1%) a partial remission was achieved. In further 11 pat. (28.2%) a stable disease and in 20 pat. (51.3%) a progressive disease during the IC was noted. The highest response rate (r.r.) of 44% was found in pulmonary lesions. Metastases of the bones were resistant to the therapy. After a mean followup time of 15.3 months, 3 pat. are alive with no evidence of disease (1 pat. due to IC and 2 pat. due to surgery of metastases after IC), 19 pat. are alive with tumor. Further 16 pat. are dead of disease and 1 pat. died of a tumor unrelated cause.

Conclusion: In contrast to recent reports in the literature, this study demonstrates, that a IC with IL-2, IFN-a and 5-FU is only of limited benefit for patients with metastatic RCC.

166 POSTER

Results and prognostic factors after surgical treatment of lung metastases in renal cell carcinoma

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Purpose: Metastatic renal cell carcinoma has a poor prognosis. In a retrospective study we examined the prognostic factors and the influence of an adjuvant therapy after resection of pulmonary metastases in renal cell carcinoma (RCC).

Methods: Between 1975–1996 42 patients (pts.) with pulmonary metastases of RCC were admitted to our department, 39 underwent surgical treatment, while 3 were not suitable for surgery. 6 pts. (14.3%) had synchronous metastases. The mean disease free interval (DFI) after nephrectomy was 32 (SD 41.3) months. Of the pts. surgically treated, 33% presented with a single lesion, 39% had two to five lesions and 28% had more than five lesions. In 61% the lesions were unilateral. 31 (82%) pts. had thoracotomy (24 pts. one stage and 7 pts. two stage), and 8 pts. (18%) had median sternotomy. With 66% atypical resection was the technique mainly used.

Results: The 5-year-survival rate of the pts. after pulmonary metastasectomy of RCC was 14%. Multivariate analysis (COX-model) for survival of preoperative risk-factors showed, that time of diagnosis (synchronous/metachronous) of the metastases ($p = 0.05$) and the number of metastases ($p = 0.01$) were of prognostic significance. Age ($p = 0.9$), localisation (uni-/bilateral) ($p = 0.36$), DFI ($p = 0.1$) and adjuvant therapy ($p = 0.7$) as a postoperative prognostic factor were of no prognostic significance.

Conclusion: In pts. with metachronous and not more than five metastases after RCC pulmonary metastasectomy should be performed. Because presence of synchronous metastases or more than 5 pulmonary metastases after RCC are unfavourable prognostic factors, indication for metastasectomy should be restricted in such cases.

167 POSTER

Intensified salvage therapy for germ cell cancer using sequential cycles of high dose carboplatin/etoposide/cyclo-phosphamide (CEC)

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The prognosis of germ cell cancer patients failing initial, cisplatin based chemotherapy is poor with an expected three years survival of approximately 20%. To improve on these results, patients were entered on a phase II protocol of sequential cycles of high dose chemotherapy. Patients received two cycles of conventionally dosed cisplatin/etoposide/ifosfamide (PEI) and peripheral blood stem cells were mobilized by GM-CSF (5 μg/kg/d s.c.). After stem cell collection, two cycles of high-dose CEC (Carboplatin 500 mg/m^2 d1–3; etoposide 400 mg/m^2 d1–3; cyclophosphamide 2500 mg/m^2 d4+5) followed by stem cell retransfusion on day 7 and GM-CSF from day 8 until hematologic recovery were administered. 28 patients have been entered; 21 in first and 7 pts in second relapse. Medium number of prior cisplatin containing cycles was 4.5 (2–10). One pt showed progressive disease while receiving PEI and was not considered for HD-therapy. 27 pts received the first cycle of CEC and 20 received both cycles. Reasons for terminating therapy after the first CEC cycle were: progression 2 pts; therapy related death 2 pts; patients refusal 2 pts; antiplatelet antibodies 1 pt. Median interval between first and second cycle of CEC was 35 days. Severe to lifethreatening toxicities, mainly infections and mucositis, were seen in all patients but did not increase in severity after the second CEC cycle. Three patients died during treatment (2 after cycle 1 and 1 after cycle 2). After a median follow up of 22.9 months (6–46 mos), 17 pts (61%) are cwithout signs of tumor progression; 3 (11%) are alive with progressive tumor and 8 (29%) have died (3 treatment-related deaths; 5 deaths from progressive tumor). These data show that two cycles of high-dose chemotherapy given 5 weeks apart are feasible in patients with relapsing germ cell tumors. Early survival data are encouraging.

168 POSTER

Paclitaxel (P) and cisplatin (C) as salvage treatment for nonseminomatous germ cell tumor (NSGCT) patients (pts)

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Based on the data that P demonstrated activity in NSGCT pts we used P 175–225 mg/m^2 3 hour infusion followed by C 100 mg/m^2 every 3 wks × 4 cycles. From October 94 to March 96 16 NSGCT pts who did not achieve a CR after C-based chemotherapy (med. number of cycles 4, range 3–6) and surgery and presented disease progression received 44 cycles of PC. From 16 pts included to the trial 13 were assessable for response and 14 for toxicity. Three pts received only one cycle of treatment and have been withdraw from the disease assessment (nephrotoxicity, refusal of the treatment, early death from the undetected brain metastases). One (8%) CR (duration 9+ mo), confirmed by retroperitoneal lymph node dissection (fibrosis and necrosis), and 3/13 (23%) PR (2 mo) were achieved. With a median follow up of 8 (1–11) mo 12 patients died from the disease progression, one is alive disease free, two are alive with disease progression and one has been lost. Median survival for the whole group was 7 mo. The toxicity was moderate: neutropenia gr. III – 29%, gr. IV – 0%, thrombocytopenia gr. I–III – 28%, creatinine >1.5 mg/%–35%, peripheral neuropathy gr. I–II – 50%, nausea and vomiting – 43%. P plus C showed a modest activity (OR rate -31%) in poor prognosis group of pts, who did not achieve a CR on induction chemotherapy.

169 POSTER

TGF-β_1 resistance as a major progression factor in human renal cell carcinoma

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Purpose: Since TGF-β_1 is a potent negative regulator of growth, we analyzed whether defects in the TGF-β_1 system might be involved in the deregulated growth of human renal cell carcinoma (RCC).

Methods: The expression of TGF-β_1 and its receptors (type I, II, III) as well as the functional intactness of the signal transduction pathways were analyzed in 30 human RCC cell lines.

Results: By ELISA, all cell lines secreted TGF-β_1 as a biologically inactive complex. RT-PCR and immunocytochemistry revealed type I ALK-5-receptor in 29 cell lines. Type II-receptor mRNA and protein could be demonstrated in all cell lines, whereas type III-receptor mRNA was observed in only 5 RCCs. Exogeneously added, biologically active TGF-β_1 (1 ng/ml) resulted in a significant ($p < 0.05$) inhibition of proliferation in 14 out of 30 RCC cell lines. In contrast, 16 RCC cell lines proved to be TGF-β_1 resistant. TGF-β_1 resistance could not be explained by mutations in two "hot spot" regions of the type II-receptor gene (bp 622–795 and bp 1868–2019) as shown by DNA sequencing.

Conclusion: A significant proportion of our RCC cell lines showed escape from negative growth control by TGF-β_1. Therefore, the acquisition of TGF-β_1 resistance has to be considered as a major progression factor for human RCCs.

170 POSTER

Bilateral testicular germ cell tumors (TGCT)

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Purpose: To study incidence, characteristics and outcome of patients (pts) with bilateral TGCT.

Methods: The charts of 29 pts with bilateral TGCT were reviewed.

Results: Among 796 pts with TGCT (1979–January 1997) 7 (0.9%) had synchronous bilateral TGCT and 10 (1.3%) developed a metachronous 2nd