

8 CCR pts, 5 are off CT/NED for 47<sup>+</sup>(20<sup>+</sup>-58<sup>+</sup>) mos and 3 relapsed and died after 13 (11-18) mos. Of 12 CPR pts, 3 were PCR and are off CT/NED for 35<sup>+</sup>(29<sup>+</sup>-40<sup>+</sup>) mos, while 9 died after 6 (3-13) mos. Total off CT/NED pts 8 (40%). Ref NED pts 2/9 (22%) and rel NED pts 6/11 (55%). Overall long term NED status with MVIP 19/38 (50%). We conclude that MVIP is very active in those very poor risk cases.

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#### ENDOCRINOLOGIC LATE SEQUELAE AFTER CHEMOTHERAPY FOR TESTICULAR CANCER

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Endocrine abnormalities regarding the androgens or estrogens and their regulatory hormones have been reported in patients (pts) after chemotherapy (CTX) for metastatic testicular cancer and may influence important cardiovascular risk factors.

**Objective and pts:** To study the influence of different CTX regimens, dosage, pts age and time since CTX on serum levels of FSH, LH, testosterone, total estrogens, estradiol, estrone, DHEA, DHEAS and 17-OH-progesterone and their correlation to serum cholesterol, liver enzymes, body mass index and blood pressure in pts treated with unilateral orchiectomy and CTX for testicular cancer. 63 pts with a median (med) age of 30 [19-53] years, and a med follow-up of 40 [16-128] months were included. Treatment: PVB: 21 pts; PEB: 22 pts; PEB + vincas: 13 pts; other: 7 pts; (P = cisplatin, V = vinblastine, E = etoposide, B = bleomycin).

**Results:** Elevated levels for LH, FSH, DHEA and 17-OH-progesterone were found in 48%, 63%, 68% and 51% of pts, respectively. 9 of 30 (30%) pts with elevated LH had low testosterone levels indicating decompensated Leydig cell insufficiency. FSH and LH levels were correlated to cumulative doses of P ( $P = 0.006$  and  $0.016$ ) and age at time of CTX. Elevated gonadotropins were found in 50% of pts after standard PEB-therapy in contrast to 82% of pts with vincaalkaloid-containing regimens ( $P < 0.04$ ). Adrenal androgens (DHEA/S) correlated to cumulative dose of P ( $P = 0.006$ ) and were significantly associated with serum cholesterol levels and body mass index in pts <40 years.

**Conclusions:** Major endocrinological abnormalities after CTX persist in >50% of the pts cured of testicular cancer. CTX-induced shifts in hormonal ratios—especially of the adrenal androgens (DHEA/S)—may be associated with elevated cholesterol levels, leading to an increased cardiovascular risk for these young pts.

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#### EXTRAGONADAL GERM CELL TUMOURS (EGGCT): EXPERIENCE AT HANNOVER UNIVERSITY MEDICAL SCHOOL

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EGGCT can arise as retroperitoneal (ret) or mediastinal (med) primary tumours. Although treated like primary gonadal germ cell tumours, their prognosis has been regarded worse.

65 patients (pts) with a median age of 28 years (18-78) treated between 1970 and 1993 at Hannover University Medical School were included into this retrospective analysis. Histology was seminoma (S) in 13 (20%) pts (4 ret; 9 med) and non-seminomatous germ cell tumour (NS) in 52 (80%) pts (26 ret, 24 med). Among pts with NS histology 58% and 60% had elevations of AFP and  $\beta$ -HCG, respectively; 76% of pts had an elevation of serum LDH. 47 pts (71%) had metastases in addition to the extragonadal primary tumour, (7 bone, 12 liver, 24 lung). Most pts were treated with either chemotherapy (CTX) alone (10 pts) or CTX + surgery (43 pts). 16 pts received additional or definitive radiotherapy. 12 of 13 pts with S (92%) achieved CR or PR; 32 pts with NS (63%) achieved CR or PR M- to initial treatment and 19 pts (37%) were failures. After a median follow up of 33 months (12-259) 10 pts with med and 13 with ret EGGCT have relapsed. 3-year overall survival for EGGCT pts with S was 78% versus 58% with NS histology. For NS pts

no significant difference in overall survival between med and ret localizations of EGGCT was found. The use of platinum/etoposide/ifosfamide-based initial CTX (22 pts) for NS pts proved to be superior to other combination regimens (35 pts) (2-year survival 76% vs 57%).

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#### CHEMOTHERAPY IN FAR ADVANCED SEMINOMA

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Since 1982 80 pts. with histologically proven seminoma have been treated with cisplatin-containing chemotherapy. All had far advanced stage of disease: 46 stage II C/D, 16 stage III, 15 stage IV. Pretreatment was administered to 30 pts, 19 with radiotherapy, 7 with carboplatin and 4 with other chemotherapy. Treatment protocol was vinblastine, ifosfamide, cisplatin (VIP) in 38 pts., etoposide, ifosfamide, cisplatin (EIP) in 33 pts., and PVB/PEB or ECBC in 6 pts. Until 3/95 66/77 pts. reached CR (86%), 15 surgically documented. 5/77 (6%) reached PR, 6/77 pts (8%) died. 2 pts. relapsed (3%) and have reached a 2nd CR. 71/77 (92%) are currently alive and show no evidence of tumor progression (median observation time 60+ months). Toxicity was high with 2 early deaths, severe thrombo- and leukopenia WHO grades 3/4, 4 severe infections and 1 tumor lysis syndrome. The EIP protocol with daily 75 mg/m<sup>2</sup> etoposide and 1.2 g/m<sup>2</sup> ifosfamide and 20 mg/m<sup>2</sup> cisplatin is our standard treatment for seminoma and is being compared to carboplatin monotherapy in the still ongoing randomized trial.

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#### IFOSFAMIDE-BASED SALVAGE CHEMOTHERAPY FOR PATIENTS WITH RESISTANT GERM CELL TUMORS—OUR EXPERIENCES

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Between 1985 and 1993, 78 male patients were treated in our Institute with germ cell tumors. All patients in Stage A, B1 and B2 were cured with PVB respectively PEB protocol—59 patients (76%). From 19 patients in Stage B3 and C, complete remission was achieved in 10 (52.6%) patients. All patients who had failed to be cured—9 (47.4%), received salvage chemotherapy (PEI protocol) consisting of cisplatin, etoposide and ifosfamide (with mesna protection). Cisplatin was given at the dosage of 20 mg/m<sup>2</sup> on days 1-5, etoposide at the dosage of 75 mg/m<sup>2</sup> on days 1-5 and ifosfamide was given at the dosage of 1.2 gr/m<sup>2</sup> on days 1-5 with mesna protection. Complete remission was achieved in 4 patients (44.4%) with chemotherapy alone in 2 patients and additional in 2 patients following by surgical resection of viable tumor. Pathohistological finding was in 1 patient necrosis and in 1 malignant tissue was present (embryonal carcinoma). This patient received one cycle PEI-protocol after surgical resection as consolidation chemotherapy. The toxicity was acceptable during the chemotherapy (all patients received adequate premedication). On the basis of our results, although only a small number of patients was included, we suggest that this protocol may be regarded as a very acceptable therapeutic procedure in the treatment of patients with resistant germ cell tumors.

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#### TREATMENT AND OUTCOME OF PATIENTS WITH EXTRAGONADAL GERM CELL TUMORS

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48 patients, 32 with abdominal and 16 with mediastinal extragonadal germ cell tumors were included in this study. 2 were women with mediastinal primaries. At presentation most patients had advanced disease. The median size of the tumors were 128 mm (abdominal) and 116 mm (mediastinal), respectively. Of the 48 patients, 14 had metastasis to liver, brain, and/or bone at time of diagnosis. Patients with metastasis to these organs had particularly poor survival. 7 patients died due to treatment-related toxicity. The median age of these seven patients were significantly higher than among the other patients. The 5-year survival of all 48 patients was 55%. 29 patients received CR after chemotherapy, determined by CT-scan and/or biopsy. 28 of these are still alive.

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