912 POSTER

SURVIVAL IN PATIENTS WITH MALIGNANT GERM CELL TUMOUR PERSISTENT AFTER CISPLATIN-BASED INDUCTION CHEMOTHERAPY

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From 1980 to 1993 about 300 patients with advanced malignant germ cell tumour underwent cisplatin-based induction chemotherapy. Post-chemotherapy histology revealed persistent viable germ cell tumour in 30 of these patients (testicular: 26; extragonadal 4). Adjuvant chemotherapy was planned in 27 patients with residual non-seminoma, and irradiation in 3 patients with resected seminoma.

Results: Eighteen patients relapsed after post-chemotherapy surgery with a median time of 5 weeks (range: 11–45). In 13 patients the relapse developed before adjuvant chemotherapy was initiated. Only 2 of the relapsing patients were cured by salvage treatment. Currently, 14 patients are alive, one of them with stable disease (5-year survival: 41%). 10 patients with elevated markers prior to post-chemotherapy surgery had an 8% 5-year survival as compared to 72% in 20 patients with normal markers. 15 patients who initially presented with small volume disease (MRC criteria) displayed a 79% 5-year survival versus 8% in patients with more extended metastases.

Conclusions: After cisplatin-based induction chemotherapy only 40–50% of the patients with a residual malignant germ cell tumour are cured, with a particularly poor prognosis in those with elevated markers before post-chemotherapy surgery or those with a large metastatic burden at the time of diagnosis. These high-risk patients should have alternative and more intensive chemotherapy before undergoing surgery.

913 POSTER

TESTICULAR DOSE AND FUNCTION AFTER PARA-AORTIC STRIP AND DOG-LEG FIELD RADIOTHERAPY FOR SEMINOMA STAGE I

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During radiotherapy of testicular seminoma, the dose to the remaining testicle should be as low as possible to preserve the patient's fertility. Two different irradiation techniques have been applied: para-aortic strip (p.a.) or dog-leg field.

Measurements of the testicular dose using the Alderson phantom to a dose of 30 Gy, show a mid-plane dose in the range of 7–13 cGy and 15–40 cGy depending on the distance of the testicle to the symphysis, for respectively the p.a. and the dog-leg field technique. In patients this distance was found to be 12 cm (mean), corresponding to a predicted testicular dose of 9.5 cGy (p.a. field) and 25 cGy (dog-leg field). This significant difference in testicular dose between the two treatment techniques, explains the reduction of sperm counts observed after dog-leg field radiotherapy, which is lacking after p.a. irradiation. The reduced spermatogenesis is accompanied by comparable changes in FSH.

914 POSTER

THE ROLE OF A CYTOREDUCTIVE SURGERY IN NONSEMINOMATOUS GERM CELL TUMOR PATIENTS WITH SMALL RETROPERITONEAL MASS AFTER INDUCTION CHEMOTHERAPY

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We identify 64 nonseminomatous germ cell tumor pts, received 4 cycles of the induction chemotherapy with VAB-6, BEP or EP, who presented a residual retroperitoneal mass (RRM) < 2 cm (med. 1.0, range 0.4–2.0), measured by an abdomen CT scan and ultrasound. All pts were marker negative and underwent a retroperitoneal dissection. The correlation of pathologic findings with a size of RRM are presented in the table.

Histology	Number of pts	Tumor size (cm)		
		<1.0	1.1–1.5	1.5–2.0
Fibrosis/necrosis	47	33*	5*	9
Mature teratoma	16	-	3	13*
Malignancy	1	-	0	1
Relapse*	3	1 (14 mo)	1 (6 mo)	21 (25 mo)

Fibrosis/necrosis was observed in all resected RRM <1.0 cm. Pts with RRM >1.0 cm frequently had teratoma and 1 pt had a malignancy. Retroperitoneal relapses occurred in 3 pts. Our data suggests that surgery could be safely avoid in a marker negative pts who presented RRM < 1.0 cm.

915 POSTER

LOW DOSE RADIOTHERAPY FOR STAGE I SEMINOMA—FIRST RESULTS

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Patients and methods: 101 patients were irradiated postoperatively for stage I seminoma. 13 received a total dose of 30 Gy in 4 weeks (single dose 1.5 Gy) mainly to the paraaortic, iliac and inguinal lymph nodes (1983–1987). Further 58 were treated with a total dose of 25.5 Gy in 3.5 weeks (single dose 1.5 Gy). The target volume was gradually reduced to the paraaortic lymph nodes only. The remaining 30 patients were irradiated with a total dose of 20 Gy in 2 weeks (single dose 2.0 Gy), the target volume was the paraaortic region only. *Results:* The mean follow-up was 3.75 years. Only two patients experienced lymph node metastases, two more distant metastases. 5-year-survival was 95.9%, 7-year-survival was 91.6%. There was no significant loss in local tumour outcome or survival due to reduction of total dose and target volume at the same time. Applying a total dose of 20 Gy (single dose 2 Gy) an increased frequency of nausea occurred. *Conclusion:* Radiotherapy of the paraaortic lymph nodes with low doses in a short overall time results in excellent survival and low side effects.

916 POSTER

WEEKLY M-BOP AS A SECOND LINE AND VIP PLUS HIGH DOSE AS A THIRD LINE SALVAGE FOR GERM CELL CANCER

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Worldwide VP 16 or vinblastine/ifosfamide cisplatin (VIP) is established as the most frequently used second line therapy for germ cell cancer with 23% of patients achieving durable complete remission (Einhorn 1992, ASCP abst 599). Several authors have developed regimens for poor risk patients giving cisplatin more frequently that q21 (eg. BOP, POMP, HIPE, BOP/VIP) though none have been as extensively tested as second line therapy as VIP. To investigate this issue 46 relapse patients have been treated with a methotrexate, bleomycin, oncovin, cisplatin (M-BOP) regimen developed from that of Wettlaufer *et al.* 1984;53:203. Treatments were given q7 for 4 weeks and then alternating 2 weeks on, 2 weeks off for a total of 8–10 treatments. 18/46 (39%) remain continuously relapse free (CRF) and 2 in stable disease for 2 or more years (11 of 31 (46%) BEP and 7 of 15 (46%) Carboplatin failures were CRF). The majority of patients failing this treatment proceeded to VIP, and more recently treated patients have received high dose treatment as consolidation (carboplatin 1200 mg/m^2 etoposide 1400–1500 mg/m^2, ifosfamide 6 g.m^2) with stem cell rescue. 9 of 27 (33%) patients undergoing 3rd line treatment achieved subsequent durable complete remission status, including 6 of 9 consolidated with high dose treatment. Currently 27 of 46 (59%) remain disease free, +2 static disease. With serious myelotoxicity less significant in BOP than VIP treated patients, and the recent failure of BOP/VIP as first line to improve over BEP, the results justify further exploration of this approach.

917 POSTER

DOSE INTENSITY IN METASTATIC NON-SEMINOMATOUS GERM-CELL TUMORS (NSGCT) OF THE TESTIS TREATED WITH FIRST LINE CISPLATIN, ETOPOSIDE, BLEOMYCIN (PEB) AND RESECTION OF THE RESIDUAL MASS

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Four courses of PEB (cisplatin 20 mg/m^2 days 1 to 5, etoposide 100 mg/m^2 days 1 to 5, and bleomycin 30 mg days 2, 9, 16 q. 3–4 weeks) or BEP (etoposide 120 mg/m^2 days 1, 3, 5) and resection of the residual mass can be considered standard therapy for metastatic NSGCT of the testis to-day. We studied the dose intensity of the PEB regimen in relation to a maintained complete remission (CR) or a continuous post surgical disease free status (NED) in 220 consecutive metastatic NSGCT of the testis treated at our institute between 1981 and 1990.

Thirty nine (17.7%) patients failed to be cured with the first line therapy, and the over all 5-year survival (Kaplan-Meier) was 90.4%. Over-all, 91 (41.4%) patients had dose reductions or a delay longer than

4 weeks. No correlation was found between average dose intensity and age; a negative correlation was found with the tumour mass (−0.16). In particular, the minimal p values were achieved with the following thresholds: 0.96 for cisplatin; 0.72 for etoposide; 0.66 for bleomycin and 0.77 for the average dose intensity. In conclusion: cisplatin cannot be reduced; the BEP schedule is using the borderline dosage of etoposide; the borderline dosage of bleomycin is two thirds of the standard dose.

918 POSTER

POSTORCHIECTOMY MARKERS ELEVATION ONLY IN NON-SEMINOMATOUS GERM-CELL TUMOURS (NSGCT) OF THE TESTIS

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Between 1980 and 1993, we observed 31 consecutive patients with persistently elevated AFP and/or HCG with normal imaging following orchiectomy for a NSGCT: 23 underwent primary retroperitoneal lymph node dissection (RPLND) and 8 primary cisplatin based chemotherapy (ChT). Twenty (87%) of the operated patients had histologically documented retroperitoneal metastases, and, of the 3 patients with negative nodes, 2 had early evidence of distant metastases and 1 had early markers normalization following RPLND (putative unrecognized retroperitoneal metastases): over-all, 9 of 23 operated patients had post operative evidence of distant metastases and another 2 received adjuvant ChT. After a median follow-up of 72 mos (range 15 to 156 mos), all 23 (100%) patients are alive disease free, 52% following RPLND alone. All 8 patients treated with primary ChT entered complete remission and 4 (50%) recurred, 1 with a resectable teratoma and 3 with cancer. After a median follow-up of 57 mos (range 23 to 133), only 6 patients (75%) are alive disease free, 50% following primary ChT alone. Both primary RPLND and primary ChT cured approximately 50% of patients, but salvage following primary RPLND was easier.

919 POSTER

"WAIT AND SEE" POLICY FOR PATIENTS WITH CLINICAL STAGE I NON-SEMINOMATOUS TESTICULAR GERM CELL TUMORS (NSTGCT)

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Goal: To investigate the frequency, time and detection of tumor recurrence.

Methods: During the period 1982–1992, 154 patients with a clinical stage I NSTGCT entered the study. After orchidectomy patients were followed by physical examination, serum tumormarkers AFP and HCG, chest X-rays and CT scanning of abdomen and chest.

Results: After median follow-up of 7 (range 2–12) years 42 patients (27.3%) had recurrent disease. All were detected within 2 years, over 90% in the first year after orchidectomy. After chemotherapy treatment for recurrence, the survival rate in the whole group was 98.7%.

Early detection by:	(%)	Site of recurrence:	(%)
AFP and/or HCG (TM)	8 (19.0)	Retroperitoneum (RP)	27 (64.2)
TM and CT	17 (40.5)	Mediastinum (M)	2 (4.8)
Only CT	16 (38.1)	Lungs (L)	2 (4.8)
Physical examination	1 (2.4)	RP and M and/or L	9 (21.4)
Chest X-rays	0 (0.0)	Inguinal lymph nodes	2 (4.8)

Conclusion: For the follow-up of patients with clinical stage I NSTGCT the wait-and-see policy is a reliable method. Probably after 5 years the follow-up can be discontinued. Chest X-rays are in the follow-up of no value.

920 POSTER

SECONDARY LEUKEMIA CAUSED BY ETOPOSIDE CONTAINING CHEMOTHERAPY IN GERM CELL CANCER PATIENTS

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Several reports have suggested that etoposide containing therapy caused a secondary leukemia in germ cell cancer pts. From December 87 to December 1993 187 pts with nonseminomatous germ cell tumors were included to the etoposide containing first-line treatment protocols (BEP, EP, EC, CEB) with a planned cumulative etoposide dose of 1440–2000 mg/m^2. The med. follow up for pts alive was 41 (13–87) mo. The follow up data are summarized in the table.

Years of follow up	Current status			
	Alive	Dead	Lost	Total
0–1	-	22	-	22
1–2	27	21	3	51
2–3	24	7	1	32
3–4	30	3*	1	34
4–5	17	-	1	18
>5	30	-		30
Total	128	53	6	187

One pt* received 4 cycles of EC (etoposide cumulative dose was 2000 mg/m^2) developed a secondary leukemia (FAB M4) 37 mo after beginning chemotherapy. He achieved a clinical remission with ara-C + daunorubicin + etoposide, but relapsed and died. In our cohort of 187 pts treated with a conventional dose of etoposide a risk of a secondary leukemia is low.

921 PUBLICATION

THE ROLE OF SERUM ESTROGENE LEVELS FOR PATIENTS WITH TESTICULAR CANCER

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In patients (pts) with metastatic testicular germ cell tumours tumour burden, sites of metastatic disease and the elevation of tumour markers AFP and β-HCG have been identified as prognostic factors. For pts with seminomas (S) no tumour markers are available. In a retrospective analysis we evaluated the possible prognostic role of serum levels for total estrogens (E), estrone and estradiol in pts with non-seminomatous (NS) or seminomatous (S) germ cell tumours.

Pts characteristics: 481 patients with a median age of 31 years (15–78) treated between 1978–88 were included. Among 155 pts with S 57 (59%) at stage I had elevated E-levels and 5 (22%), 4 (44%) and 2 (25%) pts with minimal (min), moderate (mod) or advanced (adv) disease S, respectively. Among 326 pts with NS 73 pts (60%) at stage I and 34 (39%), 11 (52%) and 32 (54%) pts with min, mod or adv disease had elevated estrogen levels, respectively. Elevated E-levels occurred most frequently with trophoblastic histology (78%) and least frequently with teratocarcinoma (42%). For pts with minimal disease (both S and NS) elevation of serum E-levels >5.5 nmol/l was the only significant prognostic factor for relapse free and overall survival. For adv disease pts elevations of E, AFP and β-HCG were independent prognostic factors for relapse free and overall survival during multivariate analysis.

Conclusion: Elevated serum E-levels without elevation of AFP or β-HCG occur in 4% (adv)—18% (stage I) of pts with NS and in 9% (adv)—59% (stage I) of pts with S. In addition to AFP and HCG-levels elevation of E-levels seem to constitute an independent prognostic factor for relapse free and overall survival.

922 PUBLICATION

INTENSIVE CHEMOTHERAPEUTIC REGIMEN WITH DOXORUBICIN, VP 16, BLEOMYCIN, CYCLOPHOSPHAMIDE, CISPLATIN (CHBEP) IN GERM CELL TUMORS (GCT)

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From 1986 to 1994, 34 patients (pts)—median age 30 yrs (range 15–56), PS 0–1, with poor prognosis GCT were treated with CHBEP. 20 pts had primary GCT of the testis and 14 pts had extragonadal GCT (EGCT). 5 pts were in 1st relapse. Pts received q21 days(d) × 3 or 4 cycles: Doxorubicin 75 mg/sqm d1, Cyclophosphamide 1200 mg/sqm d1, Bleomycin 10 mg/sqm d1-2-3, VP16 150 mg/sqm d1-2-3, Cisplatin 80 mg/sqm d1. 15 pts received rh-GCSF. 14 pts (6 EGCT, 4 GCT in 1st relapse, 4 GCT with visceral lesions) were treated after CHBEP with high dose chemotherapy (HDC) and ABMT.

Toxicity: 2 early deaths occurred; 75% pts had gr4 granulocytopenia, 40% pts had gr2–3 thrombocytopenia, 22% pts were admitted for neutropenic fever.

Results: overall response rate (RR) was 80% (2 CR, 27 PR). 28 pts achieved NED status at the completion of treatment: 20 pts with chemotherapy alone, with surgical resection of teratoma (1 pt) or residual cancer (7 pts). The median overall survival is 51 mths. For non relapsed pts, median survival is not reached (4 yrs survival: 55%).

Conclusions: CHBEP followed by HDC-ABMT seem to be an effective regimen in EGCT or GCT in 1st relapse.