901 ORAL

CONVENTIONAL AND MOLECULAR CYTOGENETIC ANALYSIS OF TESTICULAR GERM CELL TUMORS

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Conventional cytogenetic analysis of testicular germ cell tumors (GCT) revealed an isochromosome (12 p) as a specific aberration in more than 80% of cases. However, chromosome analysis is hampered by the need for short-term cell cultures and the complexity of anomalies in the mostly polyploid karyotypes. Furthermore, homogeneously stained regions and double minute chromosomes, as signs of amplification of unknown chromosomal material, are frequently found. Comparative genomic hybridization (CGH) allows the detection of chromosomal gains and losses in tumor DNA throughout the whole genome without the need for dividing cells. This method might therefore overcome at least parts of the limitations of conventional analysis. We studied DNA from fresh tissue of 10 testicular GCT's by CGH. In cases, where banding analyses where also available, both methods yielded comparable results. CGH analysis of all examined tumors showed a gain of 12p, mostly of the whole p-arm. In two tumors, an intense amplification of 12p material restricted to the chromosomal region 12p12 was found. In two other cases, gains of small chromosomal regions at 4q12 and 6p21 were also detected. Thus, these regions are highly suspicious of containing genes which may play an important role in the pathogenesis of testicular GCT's. Moreover, among other anomalies, gains of chromosomes 8, 14, 19, 21 and X as well as loss of chromosome 13 were frequent findings. In conclusion, CGH provides new insights into genetic alterations of testicular GCT's. By means of CGH, we detected chromosomal regions where amplified genes may be localized. Further investigations are necessary to confirm and to expand these findings and to identify the genes involved.

902 ORAL

OPTIMAL FIELD SIZE IN ADJUVANT TREATMENT OF STAGE I SEMINOMA

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From 7/1989 to 5/1993 478 men with seminoma stage I (T1–T3; no ipsilateral inguinal operation prior to orchiectomy) have been included in a phase III study assessing the field size of abdominal radiotherapy (30 Gy/3 wks). Group 1: paraaortic (p.a.) field from Th11 to L5, the lateral borders including the processus transversi. Group 2: "dog-leg field" (p.a. + ipsilateral iliac field to the mid obturator level).

Results: With a median follow-up time of 29 months, 114 relapses have occurred, two of them within the pelvic area (2 years relapse-free survival 97%; 95% C.I./96%, 99%). Relapses were diagnosed between 4 months and 3 years from start of radiotherapy. Acute grade ≥ 3 gastrointestinal toxicity was observed in 11% and 17% of the patients with p.a. and dog-leg field, respectively. In Group 1 grade ≥ 2 myelotoxicity occurred in 5% of the patients and in 13% of the patients from Group 2. 8 patients developed peptic ulcer after radiotherapy. After 1 year 11% patients in Group 1 and 30% of those in Group 2 were azoospermic.

Conclusions: In patients with seminoma stage I (T1–T3) and with undisturbed lymph node drainage of the primary tumour adjuvant radiotherapy to the p.a. lymph nodes is associated with reduced gastrointestinal, haematological and gonadal toxicity compared to standard pelvic + p.a. irradiation. The recurrence rate is low with either field.

903 ORAL

RISK-ADAPTED TREATMENT OF CLINICAL STAGE 1 (CS1) NONSEMINOMA TESTIS CANCER (NSTC)

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246 patients (pts) with CS1 NSTC were included into a prospective multicenter protocol during 1990–94 and treated according to 3 risk strata: Pts without tumor cell invasion of vascular structures in the testis (VASC−) and elevated serum AFP levels (AFP+) at orchiectomy were considered low risk (LR) and surveilled only. VASC− & AFP− or VASC+ & AFP+ pts were presumed intermediate risk (IR) and path. staged (PS) by retroperitoneal lymph node dissection (RPLND). VASC+ & AFP− pts were regarded as high risk (HR) and received adjuvant chemotherapy (BEP × 3) *Preliminary results at a median obs, time of 32 months:* Crude survival of all 246 pts are 100% and all relapsing pts are in remission. Of 225 fully evaluable pts: Relapse rate in the 99 LR pts are 23% and 76% had elevated serum tumor markers at relapse. One of 32 (3%) HR pts relapsed (resectable retroperitoneal mature teratoma). Of 94 IR pts 38% had either PS2 at RPLND or relapsed despite PS1. AFP status at orchiectomy had no real predictive value for subclinical metastases in this study, but may indicate increased safety during surveillance by early warning of relapse.

904 ORAL

OUTCOME ANALYSIS AFTER SALVAGE TREATMENT OF TESTICULAR GERM CELL TUMOURS

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Long-term outcome of salvage treatment was reviewed in 67 unselected patients relapsing during or after their primary cisplatin-based chemotherapy for metastatic testicular cancer. Salvage treatment predominantly consisted of cisplatin-ifosfamide-based chemotherapy ± surgery. With a median follow-up of 90 months 20 patients (30%) are alive with no evidence of disease. Prognostic factor analysis included year of diagnosis, age, primary site (testicular versus extragonadal), initial tumour burden, relative dose intensity of cisplatin, response to primary therapy, relapse-free interval, and tumour burden and marker status at relapse. Univariate analysis identified age ≤ 35 years, testicular origin, low tumour burden at diagnosis and at relapse, complete response (CR) to primary therapy and a relapse-free interval >3 months as predictors of favourable outcome. Multivariate analysis confirmed age ≤ 35, CR to primary therapy, and a relapse-free interval >3 months. Patients with these good-risk features had a 5-year survival of 72%. Prognosis for the remaining patients is poor with only 11% 5-year survival emphasising the need for innovative and more aggressive approaches.

905 ORAL

SEXUAL DYSFUNCTIONS AFTER TESTICULAR CANCER (TC)

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Introduction: 90% of pts with TC are cured. Little research is available on posttreatment sexual function (SF). Prevalences and type of sexual morbidity in TC was studied.

Methods: A questionnaire study was designed to assess SF and sent to 314 TC pts treated between 1977–94.

Results: Questionnaires returned in 84% (N = 265). Median pts age 37 (SD ± 10) yrs. Median follow-up 7 (SD ± 4) yrs. Treatment: orchiectomy + surveillance (N = 58), radiotherapy (RT, N = 45), chemotherapy (CHT, N = 28), CHT + retroperitoneal lymph node dissection (RPLND, N = 134). Impairment of SF in 116 pts (43%): reduced libido, potency disturbances, decreased orgasm and reduced/absent ejaculation were most prominent. Significant decrease in SF was present in pts with adjuvant treatment vs surveillance (24% vs 44%, $P < 0.01$). No difference in SF was present between RT-group vs CHT (+RPLND)-group. Decrease of SF in the CHT + RPLND group vs CHT alone was seen ($P = 0.08$), although pts treated with RPLND suffered more from ejaculation and potency disturbances. Deterioration in SF was observed with increasing age ($P < 0.01$).

Conclusion: High prevalence of sexual dysfunction following orchiectomy and adjuvant therapy for TC is documented in the study.

906 POSTER

MVIP CHEMOTHERAPY (CT) IN VERY ADVANCED, REFRACTORY (REF) OR RELAPSED (REL) GERM CELL TUMOURS (GCT)

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38 pts with primary GCT of the testis (35) or the CNS (3) received methotrexate (M) 250 mg/m^2 as a 24 h infusion with fol. acid d.1, cisplatin (P) 100 mg/m^2 d.4, etoposide (V) 100 mg/m^2 d. 4–6 and ifosfamide (I) 5 g/m^2 d.5 with mesna (MVIP). Of those, 18 with large/very large volume disease only (MRC staging) received MVIP as primary CT. Toxicity was considerable with no toxic deaths. There were 6 CCR + 5 CPR/PCR (61%) who are off CT/NED for $26^+(9^+–41^+)$ mos. 4 (22%) CPR pts died after 6 (3–10) mos, including 2 of the 3 CNS pts. 3 recent pts have achieved CPR so far and are still responding further. The same CT was given as 2nd line in 9 ref and 11 rel (P or carboplatin) pts. Of