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A prognostic model for response and outcome in patients with extragonadal germ cell tumors - an international multivariate analysis

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Purpose: This investigation evaluates prognostic variables in patients with seminomatous and nonseminomatous extragonadal germ cell tumors (EGCT) in order to identify relevant factors for long-term outcome following cisplatin based chemotherapy.

Methods: Patients from six countries treated in at eleven centers in Europe and United States between 1975 and 1996 were retrospectively evaluated. Multivariate analyses of prognostic variables for survival and for response to chemotherapy were performed.

Results: Data were available from 635 EGCT patients, 104 seminomas and 524 nonseminomatous EGCT (n=7 not specified). For nonseminomatous EGCT the following independent adverse factors were identified: presence of either liver [hazard ratio (HR): 1.7], lung (HR: 1.4) or central nervous system (CNS) metastases (HR: 2.5), primary mediastinal tumor site (HR: 2.3), elevation of pretreatment beta-human chorionic gonadotropin (HR: 1.5). For extragonadal seminoma no adverse feature was identified. Integration of this variables produced the following prognostic grouping: 'excellent prognosis', all seminomatous EGCT, comprising 17% with a 89% 5-year survival rate; 'intermediate high', 'intermediate low' and 'poor', all nonseminomatous EGCT with score values of 0/1, 2/3 or >3, respectively, comprising 20%, 52% and 11% of EGCT with a 69%, 55% and 17% 5-year survival rate. The decreased survival among the different groups was due to a lower rate of favourable objective remissions and a higher rate of relapses. In addition, CART modelling confirmed histology and location of primary as the major prognostic division points. Multivariate testing for the probability to respond to chemotherapy has revealed nonseminomatous histology, primary mediastinal tumor site, presence of liver, lung and CNS metastases as independent adverse factors.

Conclusion: In EGCT prognostic variables for the outcome and for response to chemotherapy could be identified which in part differ from gonadal GCT. The proposed models might help to better understand the specific prognosis of EGCT and to tailor risk-adapted treatment strategies.

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Improved survival in patients with testicular germ cell tumours

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Introduction: The treatment results in an unselected series of testicular germ cell tumours (TGCT)from a geographic area is presented.

Patients: 690 new TGCT cases were seen from 1.1 1980 to 31.12.2000 from Western Norway. After orchiectomy all patients were staged by CT scans of the abdomen and thorax (only chest X-ray for seminomas the first decade), full blood tests including the tumour markers alpha-feto protein (AFP), human choriogonadotropin (HCGbetha) and lactate dehydrogenase (LDH). We used the Royal Marsden Staging system, based on the first examination: Stage 1: tumour localised to the testicle; stage 2 abdominal lymph nodes (A: <2cm, B 2-5 cm, C>5 cm); stage 3 mediastinal or supraclavicular lymph nodes; stage Mk+ only positive markers; stage 4 distant spread). All patients with non-seminomas were treated according to the SWENOTECA II-IV protocols. Stage 1 and 2 A had a staging retroperitoneal lymphadenectomy in the first decade. Later stage 1 patiens without vascular invasion had surveillance only, while stage 1 patients with vascular invasion had 1-2 courses of the BEP20 regimen. Patients failing (defined as slow decrease of tumour markers) initial therapy in higher stages had ifosphamide added to the regimen or underwent two courses of high dose chemotherapy with stem cell support up front. Seminoma patients had gradually reduced radiation doses from 40 to 36 to 30.6 to 25.2 Gy (2 or 1.8 Gy daily) by L-fields during the periode. The last years they could chose between radiation or surveillance only. Stage 2 B and higher received chemotherapy with EP/BEP20 or PEI regimen. All cases were followed for at least 10 years except one patient who emigrated after two years.

Results: There were 382 seminomas and 308 non-seminomas. Ony 6 non-seminoma patiens died of the disease, and one from sepsis due to chemotherapy. Progressing disease or recurrence was observed in 14%. The 10-year survial rate for all patients was 98.1%. Cancer specific survival for non-seminomas was 97.1% (Stage 1:99% (n=186); Stage 2:96.6% (n=66), Stage 3 and Mk+: 100% (n=3 and 11); Stage 4:89.2% (n=42). For all seminomas the 10-year cancer specific survival rate was 99.0% (Stage 1: 100% (n=305); Stage 2: 96.3% (n=68); stage 3: 100% (n=6); Stage 4: 67% (n=3). Only 2.7% seminomas failed initial therapy.

Conclusion: Most new TGCT are currently cured by tailored therapy as a cancer specific survival in the order of 98% can be obtained in unselected patients.

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Phase II study of salvage dose-dense chemotherapy in patients with disseminated non-seminomatous germ cell tumors (NSGCT): Final results

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Purpose: To assess the efficacy and toxicity of a dose-dense alternating chemotherapy regimen in patients with refractory or relapsing NSGCT.

Methods: Chemotherapy consisted in the so-called BOP-CISCA-POMB-ACE regimen (bleomycin, vincristine, cisplatin/cisplatin, cyclophosphamide, doxorubicin/cisplatin, vincristine, methotrexate, bleomycin/etoposide, dactinomycin, cyclophosphamide) + G-CSF. Chemotherapy was recycled every 7 to 14 days and was followed by surgery.

Results: From 10/93 to 10/96, a total of 33 patients were enrolled (cisplatin-sensitive: 14, refractory: 15, absolute refractory: 4). Thirteen patients (39%) had received >1 previous chemotherapy regimen and 25 (76%) had a predicted unfavorable prognosis according to the MSKCC classification. Thirteen patients (39%) had a complete response to therapy. With a median follow-up time of 65 months (range 35–83 months), the 3-year overall survival (OS) rate was 46% (95% CI: 31%–54%) and the 3-year progression-free survival was 33% (95% CI: 21%–54%). Toxicity: G4 neutropenia (58%), G4 thrombocytopenia (61%), G4 anemia (15%), G3-4 stomatitis (30%), toxicity-related deaths (n = 2). The MSKCC classification for relapsed NSGCT seemed to allocate patients more adequately into prognostic groups (3-year OS: 75% vs 37%, $p < 0.04$) than did the MRC classification.

Conclusion: The combination of the dose-dense BOP-CISCA-POMB-ACE regimen and aggressive surgery is active as salvage therapy for NSGCT. These results compare like results of intensive regimens with hematopoietic support.

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Long term effect of oral testosterone substitution therapy on bone mineral density and hormone profil in patients with bilateral testicular cancer

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Purpose: The aim of this clinical study was to evaluate the use of long term oral testosterone undecanoate substitution therapy in patients who underwent bilateral castration due to bilateral testicular cancer.

Methods: 46 patients with primer hypogonadism were enrolled into this clinical research study. All patients received daily 2 x 80 mg testosterone undeconate as long term androgen replacement therapy. Blood samples were drawn between 8-9 am. for haematology, biochemistry and hormone measurement. Bone mineral density was obtained from all patients by single energy quantitative CT of the lumbar spines. BMD was also assessed in 25 patients on the lumbar spine and femoral neck by DEXA to compare the different methods.

Results: The mean age of patients was 40,8 years (range: 24-53) at the time of beginning of study. The mean age of patients at the time of evaluation was 40,8 years (range: 26-53) The mean age was 28,9 years (range:16-51) at the time of first castration, and 35,8 years (range: 31-51) at the time of second castration. Mean interval between appearance of the two tumors is 5,2 years. The histological diagnosis were seminoma in 21 cases, and 25 patients have non-seminoma at the time of first castration. If the first histological diagnosis was seminoma, the second testicular tumor was significantly also seminoma (P-value: 0.0000).Of the 46 subjects in the study group, two patients had testosterone levels that were within the reference