Surveillance is attractive option, avoiding unnecessary treatment, but would be even more attractive if a greater proportion of patients with occult metastatic disease could be identified and administered earlier, potentially less toxic, treatment.
A Danish pilot study in CS1 NSGCT showed that FDG PET could identify 70% of patients who subsequently relapsed, and had a negative predictive value of 90%. If confirmed this would suggest that further treatment could be avoided in most patients with CS1 NSGCT and negative PET scans.
Methods: NSGCT patients judged to be CS1 based on markers and CT, and high risk based on vascular invasion, were registered within 8 weeks of orchidectomy, and underwent an 18FDG PET scan. Following a positive scan, patients went off study and could be managed according to local protocols. Patients with negative scans were followed on surveillance. The primary outcome measure was the negative predictive value of the PET scan, defined as the 2-year relapse-free rate in patients with a negative PET scan. This was expected to be approximately 90%, and to exclude rates below 80% with 80% power, at a 5% significance level, approximately 100 PET negative patients were required and we anticipated scanning 135 patients to achieve this.
Results: Patients were registered between May 2002 and January 2005. At this time, when 116 patients were registered and PET scan results were available on 96 patients (78 PET –ve, 18 PET +ve), an independent Data Monitoring Committee review lead to early closure of the trial, due to an unacceptably high relapse rate in the PET-ve patients. PET +ve patients were slightly older than PET –ve patients (35 vs 29 yrs) and more likely to have MTU histology (83% vs 46%) and/or to have normal markers pre-orchidectomy. All PET +ve patients were scheduled for adjuvant BEP chemotherapy. One PET –ve patient requested adjuvant chemotherapy. Of the remaining 77, 23 relapsed leading to a one-year relapse-free rate of 65% 90% CI (53%, 74%). The maximum 2 year relapse-free rate (assuming complete follow-up and no further relapses) would be 70% (60%, 79%).
Conclusions: Though PET identified a proportion of patients with disease not detected by CT scan the relapse rate amongst PET –ve patients remains high. The study results therefore suggest that 18FDG PET scanning is not able to identify patients at sufficiently low risk of relapse to replace other treatment options in this setting.
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Gonadal hormones, sperm counts and post-treatment paternity in long-term survivors of unilateral testicular cancer

M. Brydøy[1,2], S. Fosså[3], R. Bremnes[4], O. Klepp[5], E. Wist[6], O. Dahl[2,1].
[1]Haukeland University Hospital, Department of Oncology and Medical Physics, Bergen, Norway; [2]University of Bergen, Section of Oncology, Institute of Medicine, Bergen, Norway; [3]Rikshospitalet-Radiumhospitalet Trust, University of Oslo, Oslo, Norway; [4]University of Tromsø and University Hospital of Northern Norway, Tromsø, Norway; [5]St. Olav University Hospital and Norwegian University of Science and Technology, Trondheim, Norway; [6]Ullevål University Hospital and University of Oslo Medical Faculty, Oslo, Norway

Background: In long-term survivors of unilateral testicular cancer (TC) post-treatment serum follicle-stimulating hormone (s-FSH), serum testosterone (s-tes) and sperm counts were analysed according to previous treatment and associations with post-treatment paternity were assessed.
Material and methods: In 1998–2002 TC patients treated 1980–1994 in Norway were followed-up by a questionnaire, clinical examination and laboratory assessments. Of 1687 eligible men under 65 years without androgen replacement, serum hormones were analysed in 1198 (median follow-up 11 years, age 43 years). 348 delivered a semen sample. Patients were grouped according to treatment: Surgery only (Surg, n = 236), radiotherapy only (RT, n = 487), and two chemotherapy groups, [Cisplatin (Cis) $\leqslant$850 mg, n = 385 and Cis >850 mg, n = 90].
Results: S-FSH was elevated ($\geqslant$12 IU/l) in 42% of the men: Surg, 31% (median 8.8 IU/l); RT, 37% (9.7 IU/l); Cis $\leqslant$850 mg, 47% (11.1 IU/l) and Cis >850 mg, 77% (20.2 IU/l) ($p < 0.001$). In a linear regression model, age, cryptorchism and treatment group were significant factors for logarithmic s-FSH ($p < 0.001$), but with no difference between the RT and Surg group. In a linear regression model including age ($p < 0.001$) and cryptorchism ($p = 0.14$), s-tes was significantly lower in all treatment groups compared to Surg ($p = 0.02$). Sperm counts were <20 mill/ml in 49%, and <10 mill/ml in 36%. The frequency of azoospermia varied from 10% (Surg) to 43% (Cis >850 mg). In a proportional ordinal logistic regression for increasing levels of sperm counts (0, 0.1–1.9, 2.0–9.9, 10.0–19.9 and $\geqslant$20 mill/ml), adjusting for age and cryptorchism, the odds ratios compared to surgery were: RT, 0.74 (95% CI 0.43–1.27); Cis $\leqslant$850 mg, 0.51 (95% CI 0.29–0.89); and Cis > 850 mg, 0.20 (95% CI 0.08–0.52). Overall, 488 had tried to conceive a child following treatment. The median s-FSH value was 8.7 IU/l in those who succeeded (n = 330) vs. 12.8 IU/l in those who failed (n = 157) ($p < 0.001$). Respective s-tes values were 15.2 vs. 14.2 mmol/l (NS) and median sperm counts were 32 vs. 4.2 mill/ml ($p = 0.004$). In a Cox regression model where logarithmic s-FSH, s-tes and cryptorchism were assessed for their association with post-treatment paternity, only s-FSH remained an independent factor ($p < 0.001$). In men whose semen was analysed, both sperm count and s-FSH ($p = 0.03$) were significantly associated with post-treatment paternity.
Conclusions: Post-treatment spermatogenesis evaluated by post-treatment s-FSH and sperm counts was impaired in 42–49% of long-term survivors of TC and was associated with paternity after treatment. RT did not significantly impair long-term spermatogenesis compared to surgery, whereas chemotherapy did, with more severe suppression at the higher doses. Cytotoxic treatment significantly reduced s-tes as compared to surgery alone, but no association was observed between post-treatment paternity and s-tes.

Oral presentations (Tue, 1 Nov, 9.15–11.15)
GU – new frontiers in genitourinary cancers

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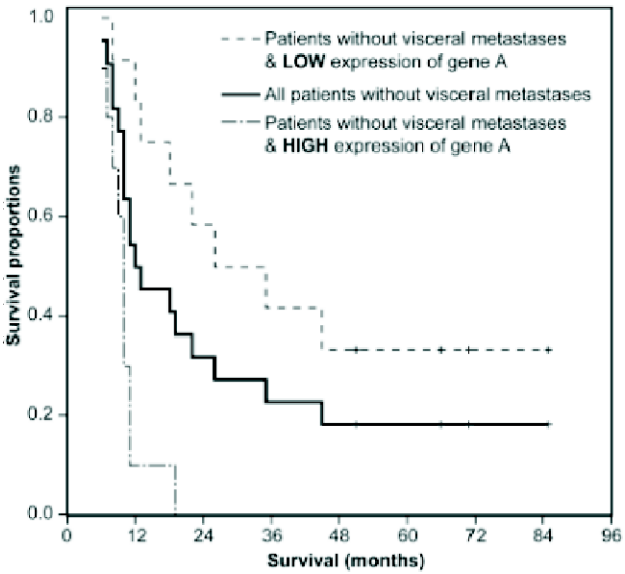
Molecular prognostic markers for survival after chemotherapy in advanced bladder cancer

A.B. Als[1], K. Koed[2], J.L. Jensen[2], L. Dyrskjot[2], T.F. Orntoft[2], H. von der Maase[3]. *[1]Aarhus University Hospital, Department of Oncology, Aarhus, Denmark; [2]Aarhus University Hospital, Molecular Diagnostic Laboratory, Department of Clinical Biochemistry, Aarhus, Denmark; [3]Aarhus University Hospital, Department of Oncology, Aarhus, Denmark*

Background: In patients with advanced bladder cancer, cisplatin-containing chemotherapy yields response rates around 50%, with a median survival around 12 months. Poor performance status (PS $\geqslant$ 2) and presence of visceral metastases are identified as independent poor prognostic factors for survival in several studies. However these factors are not strong enough to predict the outcome for the individual patient.
Aim: To identify differentially expressed genes with a prognostic impact on survival after the cisplatin-containing regimens MVAC (methotrexate, vinblastine, doxorubicin, and cisplatin) or GC (gemcitabine and cisplatin).
Material and methods: We identified 31 patients with a follow-up time of more than 15 months following MVAC or GC. Tumor biopsies were sampled less than four months prior to chemotherapy. Gene expression data were generated using Affymetrix GeneChip HU133A. Genes that correlated significant with survival were identified using SAM (Significance Analysis of Microarrays; Stanford University Labs).



Survival of patients with advanced urothelial cancer without visceral metastases according to expression values of gene A.

Results: Thirty-nine genes correlated highly significantly with survival. We selected five genes well annotated and with intelligible biological relevance for further analyses. The genes encode proteins involved in apoptosis regulation, DNA-damage-repair upon chemotherapy, cell-proliferation and angiogeneses. Expression values were dichotomized and analyzed in combination with clinical prognostic factors. Patients with (n = 9) or without