Poster presentations (Tue, 25 Sep, 09:00–12:00)
Genitourinary malignancies – prostate cancer

4006 POSTER

Gene profile predicts protection from radio-induced late rectal bleeding in prostate cancer

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Background: Despite the recent sophistication in technology, 5–10% prostate cancer patients (pts) treated with radiation (RT) can still suffer from significant morbidity (tox). Recent findings show abnormal transcriptional responses to DNA damage as associated to acute tox. We tried to identify genetic markers correlated with late rectal bleeding (lrb) in prostate cancer pts treated with 3D conformal RT and selected within the AIROPROS 0101 trial, activated to analyze the correlation between lrb and dosimetric variables.
Materials and Methods: EBV-immortalized lymphocytes (LCL) obtained from blood samples from 30 pts (⩾70–76 Gy CRT; min f-up: 24 mos) and 10 healthy donors were analysed: low risk group [V70 < 15% and V50 < 45%]: 10 pts with G2–3 lrb ("radio-sensitive" pts); high risk group (V70 > 25% and V50 > 60%): 10 pts with G2–3 lrb; high risk group: 10 pts showing no tox ("radio-resistant" pts). Quantitative RT-PCR was performed on each pt, partly irradiated using a 137Cs source (5 Gy), partly left untreated. Inter- and intra-group expression levels with and without RT and class prediction were compared using the BRB ArrayTools, at $p < 0.05$.
Results: 75% of the genes analyzed were RT modulated in at least one of the 4 groups (intra-group comparison). Most of the genes were induced by treatment in all groups but the "resistant", where 4 of the 10 modulated genes were decreased by RT. The other groups presented 18–21 modulated genes, mainly RT induced. The "resistant" and the "sensitive" groups showed many differences before treatment (inter-group comparison) and 10 genes were significantly higher in the "resistant", suggesting a protection from adverse reactions. Only 3 genes were modulated after treatment. Most genes were expressed at the same levels in untreated "resistant" pts and in all the other groups after RT, suggesting their constitutive activation in the "resistant" pts. One of the identified genes was able to distinguish resistant pts from the others.
Conclusions: Pts exhibiting no lrb showed several genes with higher basal levels than other pts/donors. One of these genes might be considered as a potential predictor of late toxicity protection. If validated these results might enable clinicians to use more "flexible" DVH constraints and/or to safely deliver higher RT doses.
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4007 POSTER

Molecular and functional profiling for an improved clinical management of prostate cancer

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Background: Prostate cancer (PCA) is the most frequent tumor type in males and a major cause of death due to malignancy. The widespread use of the prostate specific antigen (PSA) for the detection of PCA has resulted in an increasing number of men diagnosed with organ-confined, low Gleason-score PCA. However, the high sensitivity of the PSA test is accompanied by a low specificity, causing many patients suffering from unnecessary biopsy taking. Thus, the major aim in current PCA research is to find new molecular markers to improve early diagnosis, prediction of progression, and therapy of PCA.
Materials: To screen for such markers, we applied the cDNA microarray technology to examine genome-wide differences in gene expression in various prostate tissues.
Results: In a first study, we compared normal and tumor prostate from PCA patients. All samples were microdissected and quality-checked before enrollment into the study. We found a large number of differentially expressed genes, including known markers as well as genes whose association with prostate cancer has not been described before. We validated the gene expression patterns of selected candidates with quantitative RT-PCR (qRT-PCR) and derived a gene expression signature for tumor diagnosis and progression. Functional analysis of selected genes by RNA interference in prostate cancer cells revealed several genes, which were conspicuous in cell invasion assays. A second microarray study was designed to compare normal prostate tissue from healthy volunteers to histologically benign tissue from PCA patients. The results were validated by qRT-PCR on an independent sample set taken from tumor-free biopsies.
Conclusions: From these analyses, we derived a diagnostic gene signature, which may be useful to improve patient counseling after negative prostate biopsies, i.e. immediately extended re-biopsy vs. watchful waiting.

4008 POSTER

Bevacizumab/interferon-alpha2a provides a progression-free survival benefit in all prespecified patient subgroups as first-line treatment of metastatic renal cell carcinoma (AVOREN)

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Background: Immunotherapy is the current standard of care for patients with metastatic renal cell cancer (mRCC), however only patients with good prognosis typically derive a clinical benefit.Bevacizumab (BEV, Avastin®) is a humanised monoclonal antibody that inhibits tumour angiogenesis by targeting vascular endothelial growth factor. Phase II trials have demonstrated that BEV provides a clinical benefit in both untreated and previously treated patients with mRCC. A multicentre, randomised, double-blind, phase III trial was conducted to compare the efficacy and safety of BEV in combination with interferon (IFN)-α 2a (Roferon®) as first-line treatment in mRCC.
Materials and Methods: Eligible patients had: confirmed clear cell mRCC, undergone nephrectomy, Karnofsky performance status ⩾70%, no CNS metastases, no prior systemic therapy and adequate organ function. Patients were randomized in a 1:1 ratio to IFN-α 2a plus BEV or placebo, stratified by country and Motzer score. Treatment consisted of IFN-α 2a at a recommended dose of 9 MIU 3x/week for up to 1 year, plus BEV 10 mg/kg q2w or placebo until disease progression. Tumour assessments were performed every 8 weeks until week 32 and every 12 weeks thereafter. The effects of baseline demographic and prognostic patient characteristics on progression-free survival (PFS) were analyzed. Cox's proportional hazards model was used to analyze PFS for each level of the baseline variables.

Category	Subgroup	n	Hazard ratio
All		649	0.63
Age	<65	410	0.54
	⩾65	239	0.77
Gender	Female	193	0.60
	Male	456	0.64
Motzer score	Favourable	109	0.77
	Intermediate	433	0.53
	Poor	64	0.69
Lung metastases	No	173	0.77
	Yes	473	0.58
No. of metastatic sites	⩽2	394	0.67
	>2	252	0.54
Body weight loss	⩽10%	501	0.58
	>10%	81	0.76
Baseline VEGF	Below median	191	0.45
	Above median	191	0.67

Results: Between June 2004 and October 2005, 649 patients were randomised (641 treated) at 101 centres in 18 countries. Baseline characteristics were similar in both groups. With a median follow-up of