Poster presentations (Mon, 21 Sep, 14:00–17:00)
Genitourinary malignancies – Other

7161 POSTER

Stage I seminoma: can 18Flurorodeoxyglucose positron emission tomography (FDG-PET) predict occult dissemination? Preliminary results of a phase II study

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Adjuvant radiotherapy, adjuvant chemotherapy, and surveillance with treatment in case of a relapse, with high cure rates of 99–100% being achieved, whatever the option. With the evidence of long-term toxicity, sparing useless treatment has become a priority in patients with stage I seminoma. FDG-PET was demonstrated to be an accurate technique to evaluate post-chemotherapy residual masses in patients with advanced seminoma. Therefore, we evaluated the utility of FDG-PET to identify occult dissemination in stage I seminoma.
Patients and Methods: After orchiectomy and a signed informed consent, patients with testicular seminoma and no evidence of metastases on CT scan of the pelvis, abdomen, and thorax (stage I) underwent a PET-CT. PET-negative patients were offered surveillance or adjuvant treatment by radiotherapy or chemotherapy.
Results: 56 eligible patients participated to this program from March 2004 to June 2008. Six patients (11%) had a positive PET-CT, with abnormalities in the retroperitoneum. These 6 PET-positive patients were treated by either immediate (n = 4) or differed (after a rapid relapse, n = 2) chemotherapy and none relapsed thereafter. Among 50 PET-negative patients, 7 requested adjuvant chemotherapy and did not relapse. Of the remaining 43 PET-negative patients, 5 relapsed, all in the retroperitoneum, with a delay of 6, 8, 10, 16, and 18 months respectively. These patients achieved a continuous disease-free status after radiotherapy (n = 1) or chemotherapy (n = 4). With a median follow-up of 31 months, the overall survival rate is 100%.
Conclusion: This study confirms that post-orchiectomy treatment can be avoided in a majority of patients with stage I seminoma. It also suggests that PET-CT may help identifying about half (6/11) patients with disseminated seminoma that was not detected by CT-scan. Pending validation, PET-CT may therefore help better selecting patients that are candidate for surveillance.

7162 POSTER

Post-chemotherapy residual masses <15 mm in patients with metastatic non seminomatous germ cell tumors: is resection required?

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Background: Management of patients (pts) with metastatic non seminomatous germ cell cancer (NSGCT) with residual masses <15 mm in diameter after cisplatin-based chemotherapy is controversial although retroperitoneal lymph node dissection (RPLND) is usually advocated.
Methods: Data from all pts with stage II-III NSGCT treated with cisplatin-based chemotherapy from 1991 to 2008 at IGR were collected. Pts with residual mass <15 mm managed by careful surveillance were reviewed.
Results: Sixty two pts (BEP = 43; EP = 15; others = 4) fulfilled these criteria. The median age was 29 years (15–47). According to the IGCCCG classification, pts were initially classified as good- (n = 52), intermediate- (n = 6), and poor prognosis (n = 4). All pts had retroperitoneal lymph node metastases with a median diameter of 20 mm (range10–160 mm) before chemotherapy. After chemotherapy, the median diameter of residual masses was <5mm (n = 39), 5–10 mm (n = 10), 10–15 mm (n = 12). With a median follow-up of 5 years, 3 pts experienced a recurrence (4.8%), including two with relapse in the retroperitoneum (3%), who were subsequently rendered long-term disease-free by chemotherapy and surgery, and 1 with a brain relapse without retroperitoneal relapse. No late relapse was observed.
Conclusions: Pts with residual masses <15 mm after primary chemotherapy for metastatic NSGCT may be managed without systematic post-chemotherapy surgery. This data requires confirmation by other groups.

7163 POSTER

Phase II study of eribulin (Halichondrin B analogue, E7389) in patients with advanced urothelial cancer (AUC) – California Cancer Consortium led NCI/CTEP-sponsored trial

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Introduction: There is a major unmet need for efficacious non-platin drugs in AUC, particularly for patients with renal dysfunction. Microtubule directed agents (taxanes) have activity in UC. We previously undertook a first in human phase I study of eribulin, a microtubulin modulator derived from black Pacific sea sponge toxin (T. Synold, ASCO A2054, 2005); <10% of eribulin/metabolites are renally excreted. Encouraging activity was evident in AUC. Phase II dose was 1.4 mg/m^2 in a weekly dose schedule.
Methods: The phase II component of this study accrued patients with normal creatinine or calculated CrCl $\geqslant$59 mL/m, AUC: any histological type & no prior cytotoxic therapy for advanced disease (neo/adjuvant allowed). Eribulin 1.4 mg/m^2 was given IV on d 1 & 8, 3-week cycle. Endpoints: response rate (RR) >20% was deemed interesting in a 2-stage design requiring $\geqslant$2 responses/21 pts to proceed to total 41 pts; PFS and OS.
Results: In the phase II component, 40 pts evaluable: 35 with TCC, 3 adeno, 1 SCC and 1 small cell AUC. Median age: 66.2 yrs (37.4–86.8); 68% male; KPS $\geqslant$90% in 60%, $\leqslant$80% in 40%. 72.5% had prior neo/adjuvant chemotherapy. Bajorin risk groups: 0: 25%, 1: 48%, 2: 28%. Response criteria: 1 CR +13 PR from 40 pts assessable, RR 35% 95% CI: (21%, 52%). In addition, of 10 pts with SD as best response, 2 pts had uPR on 6 wk scans only to have PD at 12 wks. All responses occurred in pts with TCC (RR 40% in this subgroup). At median follow-up 15.8 months, median PFS 3.9 months (2.7, 5.1; 35 pts progressed), median OS 10.0 mo (7.0, 17.4; 19 pts dead). PFS was associated with Bajorin risk group (p = 0.01 for trend). 20 pts experienced Gr 3/4 neutropenia, no febrile neutropenia. Sensory neuropathy: 23 pts (22 Gr 1/2). Other non-hematologic toxicities: hyperglycemia, hyponatremia, alopecia, leg fatigue & aching. In a concurrent phase I study in renal dysfunction, pts with CrCl 40-–59 mL/m tolerated 1.4 mg/m^2 without DLT and accrual is ongoing for pts with CrCl <40 mL/m.
Conclusions: Eribulin has activity in AUC at doses tolerated by patients with normal, moderate & severe RD. Further analysis will be undertaken to place these phase II data in historical context especially pertaining to Bajorin prognostic criteria and prior neo/adjuvant therapy, which is associated with OS ~6 months (Dorff TB et al WJU 27:39, 2009). Early reports of responses to eribulin are encouraging esp given its limited toxicity to date.
Support: NCI Grant U01CA062505.

7164 POSTER

A prospective study of cognitive function in testicular cancer patients – preliminary results

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Background: Based on cross-sectional studies it has been discussed if systemic chemotherapy may have negative impact on cognitive function in some testicular cancer patients (TCPs). So far no relevant prospective study of cognitive function in TCPs has been published. We report preliminary results from such an ongoing prospective study.
Material and Methods: At baseline 129 newly diagnosed TCPs (median of 35 days after orchidectomy; before start of any additional treatment) were tested with a neuropsychological test battery with a total of 18 measures across different domains of cognitive function. So far 78 TCPs have been re-tested at follow-up at a median of 13 months after end of treatment; 23 TCPs received no chemotherapy (surveillance or radiation only; group 1), 27 TCPs received one cycle of chemotherapy [one treatment with carboplatin or one cycle with bleomycin, etoposide and cisplatin (BEP);

group 2] and 28 TCPs received ⩾2 cycles of chemotherapy (⩾2 cycles with BEP or EP; group 3). An individual change in performance from baseline to follow-up on each neuropsychological test measure was assessed using a standardized regression-based model (SRB), fitted first to group 1 (reference). All test scores at follow-up were compared to their predicted values using this SRB-model. The SRB-model could not be applied for skewed test scores (4 out of 18 test measures) and these test scores were categorized, and an individual change of category from baseline to follow-up was registered. Based on all these analyses, the individual overall change in neuropsychological test performance from baseline to follow-up was classified as either "no change", "improved" or "declined".
Results: We found no statistically significant difference between the three groups in the proportions that exhibited decline or improvement on neuropsychological test performance. Data from all patients evaluated at follow-up until September 2009 (approx. 90% of the included TCPs) will be presented at the congress.
Conclusions: Our preliminary results do not support the hypothesis that systemic chemotherapy may affect cognitive function in TCPs; however type II statistical errors cannot be excluded.

7165 POSTER

The value of PET/CT with F-18-FLT and F-18-FDG in the therapeutic management of metastatic germ cell tumours

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Background: To assess the ability of F-18-FLT ([F-18]-3'-Fluoro-3'-deoxythymidin), a cell proliferation marker, for early response monitoring and prediction of histology of residual tumor masses in patients (pts) with metastatic germ cell tumors (GCT) in comparison to the standard tracer F-18-FDG (2-fluoro-2-deoxy-D-glucose), CT scans and serum tumor markers.
Material and Methods: Eleven male patients (pts), aged between 23 and 48 years, with metastatic GCT were evaluated with both F-18-FDG-PET/CT and F-18-FLT-PET/CT prior to chemotherapy (CTh), after the first cycle (early response) and 3 weeks after completion of induction CTh. PET was analyzed retrospectively visually and quantitatively. The results were validated by histopathology of resected residual masses after CTh in 7 pts or by clinical-radiological follow-up for at least 6 months in 4 pts. Presence of necrosis was judged as responder, as well as CR/PRm- within a minimum progression-free interval (PFI) of 6 mos. In case of multiple resections, the worse histology was taken into account. Regarding early tumor response EORTC criterias were used.
Results: Eight out of 11 pts had a PFI >6 mos (range, 206−1337 days). Examination of resected masses revealed necrosis in 3/7, teratoma in 2/7 and viable tumor in 2/7 pts. Prior to CTh the reference lesions showed increased FDG uptake ($SUV_{mean/range}$ 8.8/2.9−15.0) in all pts but moderate FLT uptake ($SUV_{mean/range}$ 3.7/1.7−9.7) in 10 out of 11 pts. Decrease of SUV_{mean} after 1 cycle of CTh was 64% in responders and 60% in non-responders (p=.8) for FDG, as well as 58% vs. 48% for FLT (p=.5), respectively, and 85% vs. 73% (FDG, p=.1) and 68% vs. 65% (FLT, p=.8) in the final monitoring. Results of early and final response were inconsistent in 6/11 pts in FDG and in 4/10 pts in FLT-PET. The 2 pts with teratoma presented false negative results in both FDG- and FLT-PET. The sensitivities, specificities, positive and negative predictive values (%) of FDG- and FLT-PET for early and final response monitoring were 60/33/43/50, 60/80/75/67, 20/100/100/60 and 0/100/0/50, respectively.
Conclusions: PET negative residual masses after CTh of metastatic GCT still require resection, since the low negative predictive value of F-18-FDG-PET cannot be improved by application of the proliferation marker F-18-FLT.

7166 POSTER

Predicting and preventing thrombo-embolic events in patients with germ-cell tumors receiving cisplatin-based chemotherapy

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Purpose: We previously demonstrated that patients with germ-cell tumor (GCT) receiving cisplatin-based chemotherapy are at a high risk of thrombo-embolic event (TEE) compared to patients of a same age with other cancers and receiving a similar treatment. Serum lactate dehydrogenase (LDH) and body surface area (BSA) were identified as independent predictive factors for TEE (Piketty et al. Br J Cancer 2005; 93: 909−14). The aim of this study was to prospectively validate these predictive factors and to assess the impact of a thrombo-prophylaxis policy in patients at risk of TEE.
Patients and Methods: From 2001 to 2007, 144 patients received first-line cisplatin-based chemotherapy for GCT at Institut Gustave Roussy. Preventive anticoagulation with low molecular weight heparin was recommended in patients with elevated serum LDH and/or BSA > 1.9 m^2. Incidence of TEE during the 6 months following the initiation of chemotherapy was assessed. Ten patients with evidence of TEE before starting chemotherapy were excluded from the analysis.
Results: Among 134 eligible patients, a TEE occurred in 16 (12%) including deep venous thrombosis (DVT) (n = 9) and superficial thrombophlebitis (STP) (n = 7). The incidence of TEE was 14% in 92 patients with one or both risk factors (9 DVT and 4 SVT) and 7% (3 STP) in the 42 patients with no risk factor. Of note, all 9 DVT occurred in patients with risk factors (9% vs 0%). Most (6/7) STP were located in the patients'arms used for peripheral venous access. The outcome was favorable in all 7 STP. Overall 24 patients (26%) with risk-factors received primary thromboprophylaxis, and this rate increased with time and with the availability of the results of our previous study (Br J Cancer 2005; 93: 909−14): 18% and 38% before and after 2005, respectively. The incidence of DVT slightly decreased from 11% to 8% during this period, respectively. Thromboprophylaxis was not associated with haemorrhage toxicity in this population.
Conclusion: This study confirms that patients with GCT receiving chemotherapy and either elevated serum LDH or a high BSA or both factors are at risk of developing TEE, specifically DVT. The use of a primary thromboprophylaxis was feasible in these patients and its systematic implementation is now an ongoing process in our institution.

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Adjuvant chemotherapy (ACT) in patients with invasive bladder carcinoma (IBC): multivariate analysis of a cohort study

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Background: The use of ACT for IBC is only supported by retrospective nonrandomized studies or underpowered randomized trials. Additional information from metanalysis or observational studies can help to better define its role.
Patients and Methods: Since 1988, our institutional policy for patients (p) with IBC who underwent radical cystectomy (C), was to offer ACT to those patients who agree after they have been informed about their risk factors for relapse, toxicity of ACT, and status of the art at that moment. P treated with C or C+ACT were then followed according to the standard clinical practice. In this study we have retrospectively collected data in order to analyze the effect of ACT on the outcome of these two cohorts.
Results: From 1988−2008, 447 p having a radical cystectomy for IBC were identified (277 only C, 170 ACT). Chemotherapy consisted of 3 courses of MVAC (90 p) or, mainly from year 2000, 4 courses of CDDP 70 mg/m^2 d1 – gemcitabine 1 gr/m^2 d1,8 (73 p) or carboplatin – gemcitabine (7 p). There were no toxic deaths. Median follow-up was 63 m. As expected, there was a clear unbalance against the ACT cohort respect to important prognostic variables. Thus (C vs ACT): AJCC 2002 staging (pII, pIII, pIV: 56.7%, 33.6%, 9.7% vs 18.2%, 32.9%, 48.8%); histology (papillary/solid: 41.5%/58.5% vs 21%/79%), grade (G3: 91% vs 96.5%), surgical complications (39 % vs 28%) andperiod of treatment (until 1999/2000 and later: 57%/43% vs 39%/61%); p < 0.05 for all comparisons. Age was unbalanced in the pIII subgroup; 90% were male in both groups. Despite that, there were no statistically significant differences either in crude progression-free survival (PFS), overall survival (OS) or cancer-specific survival (CSS) in both cohorts. A multivariate Cox analysis including the above variables was fit to estimate the hazard ratio (HR) of relapse and death (ACT/C). We found interaction between stage and type of treatment, so results are presented stratified by pathological stages in the following table:

	PFS		SCS		OS	
	HR	95% IC	HR	95% IC	HR	95% IC
Unadjusted	1.18	0.9−1.6	1.10	0.82−1.50	0.98	0.76−1.27
Multivariate						
pII	1.01	0.53−1.91	0.88	0.42−1.8	0.77	0.42−1.43
pIII	0.58	0.35−0.96	0.64	0.37−1.1	0.55	0.34−0.88
pIV	0.28	0.16−0.50	0.31	0.16−0.60	0.28	0.15−0.50