'b' and 'c' samples were significantly higher than in the 'a' samples at the first instillation ($p < 0.01$). The Kruskall-Wallis test resulted in a significant difference of mean sICAM-1 levels at the 6th instillation between responders and non responders ($p < 0.05$). Regression analysis showed significant correlation between ICAM-1 levels at the 6th instillation and response to treatment. This correlation was not dependent on the type of administered immunotherapy. By setting a cut-off value of 338.2 ng/mL, ICAM-1 sensitivity was 85%, specificity 84.6% and negative predictive value was 88.5%.
Conclusions: Soluble ICAM-1 urine levels at the 6th instillation seem to be an independent predictor of response to intravesical immunotherapy with high sensitivity and specificity. Correlation with disease progression would require a larger patient population and is currently in progress.

872 POSTER

10 year experience in using a modified field size in hemibody irradiation for metastatic prostate cancer

F.A. Bashir, P.M. Windsor. *Ninewells Hospital and Medical School, Clinical Oncology, Dundee, United Kingdom*

Introduction: This retrospective review was carried out to assess whether patients receiving modified hemi-body irradiation (HBI) required further treatment to sites outwith the radiation field, namely the skull and lower leg, and whether the treatment outcome was successful – in terms of pain control, or subsequent treatment for pain or new skeletal events within the treated area.
Method: 103 patients with widespread bony metastases from prostate cancer received modified HBI in a consecutive 10 year period, using the same radiotherapy (RT) technique and dose. The treatment field for the upper hemi-body excluded the region above the ramus of the mandible, and for the lower hemi-body the region below the knee was excluded. A successful outcome of HBI was determined by assessing whether pain was better, the same or worse in combination with any change in analgesia intake. This was assessed for the first outpatient review at 6 weeks post HBI and again at the final documented outpatient follow up to see whether the successful outcome was sustained.
Results: 45 patients received sequential (upper and lower) modified HBI, of whom 33/45 patients (73.3%) had a successful outcome at their first review (87.9% sustained this success at last review), with only 3/45 patients receiving further RT to the skull (2/45) and lower leg (1/45). 20 patients received upper modified HBI alone, of which 17/20 patients (85%) had a successful outcome at first review (94.1% sustained this success at last review), with no RT required to the skull. 38 patients received lower modified HBI alone, of which 26/38 patients (68.4%) had a successful outcome at first review (80.8% sustained this success at last review), with no further RT to the lower leg. Toxicities were minimal, with 6/103 patients experiencing nausea, 1/103 had diarrhoea, and pneumonitis was not seen. Post HBI, 25/103 patients (24.3%) required a blood transfusion while no patients required a platelet transfusion. 5/103 patients (4.8%) developed new skeletal events in the treated area.
Conclusions: HBI provides successful and sustained relief in the majority of patients with bone pain in metastatic prostate cancer. Modifying the field size, as not to include the skull and lower leg, does not appear to have any significant impact on the final outcome of treatment, namely pain control and the need for additional RT. A low incidence of side effects was associated with modifying the field size, for the patients reported here.

873 POSTER

Organ preservation in urinary bladder cancer: conservative treatment with radiochemotherapy for fragile patients. Mono-institutional experience.

M. Soler Tortosa[1], J.L. Monroy Anton[1], A. Navarro Bergada[1], M. Lopez-Muñoz[1], A. Benedicto[2], C. Reig[2], J. Cuevas Sanz[2]. [1]*Hospital De La Ribera, Radiation Oncology, Alzira (Valencia), Spain;* [2]*Hospital De La Ribera, Urology, Alzira (Valencia), Spain*

Introduction: Conservative treatment allows the anatomical and functional organ preservation in some oncology patients. In this way, there are some radiochemotherapy protocols in the treatment of muscle-invasive urinary bladder cancer. They can conduce to a similar survival of patients, with vesical conservation without cystectomy in great number of the same.
Purpose: to assess the efficacy of a multidisciplinary treatment protocol for muscle-invasive bladder cancer in fragile or elderly patients. The protocol comprising rigorous transurethral resection (TUR) and chemo-radiotherapy, evaluating local control and survival.
Patients and methods: thirty six patients treated in the period 2002–2004, aged mean 70 years (49–78) were enrolled in this study. All of them with a diagnosis of muscle invasive bladder cancer stage: T2a-T4a. The treatment protocol consisted on maximal TUR of the bladder tumors, followed by two cycle's chemotherapy with Carboplatin plus Gemcitabine, administered previous conformal 3D radiation therapy: 45 Gy on pelvis volume and total dose of 65 Gy in bladder, concomitant with a weekly dose of carboplatin (total dose of 50 mg) as radio sensitizer. Response was evaluated by restaging transurethal resection. Cystectomy was considered when persistent tumour or local relapse was achieved.
Results: with a median follow-up of 31 months (ratio 8–44), actuarial 3 years cancer specific and overall survival rates are 70% and 61%. Conserve the bladder 89% (32/36) and 87% (28/32) of them are free of local relapse. Two patients underwent early cystectomy because of no response, and two patients underwent delayed cystectomy. The combined treatment is excellently tolerated and therefore with high index of fulfilment (79%). Toxicity has been very low.
Conclusions: the results of this study show that bladder-sparing radiotherapy with neoadyuvant and concurrent chemotherapy is feasible in elderly or fragile patients (mean aged of 70 years) with excellent results in terms of local control and survival. Most of them can conserve functional bladder without important side-effects.

874 POSTER

Gemcitabine monotherapy in the treatment of locally advanced/metastatic bilharzial-related bladder cancer: a follow up report

Y. Mostafa Kamel, H. Zawam, H. Moharam, A. Fouda. *Clinical Oncology Department, Cairo University, Cairo, Egypt*

Background: In Egypt, bladder cancer represents 18.2% of all cancer types. Its high incidence is potentially related to the domestic prevalence of bilharziasis, which causes pathologic changes rendering this disease more resistant to chemotherapy and radiotherapy. The activity of gemcitabine in transitional cell carcinoma (TCC) is well studied in western countries; therefore, we conducted this phase II study to evaluate the efficacy of gemcitabine in locally advanced/metastatic bilharzial-related bladder cancer.
Methods: Eligible patients had locally advanced/metastatic (T3b, T4/N2–3/M1) bilharzial-related bladder cancer, were aged 18–75 years, and had WHO performance status (PS) of 0–2. No prior chemotherapy or radiotherapy was allowed, but prior surgery was acceptable if disease recurred. Adequate bone marrow reserve and organ function, a life expectancy >6 months, and informed consent was required. Patients received gemcitabine 1200 mg/m^2 via 30-minute infusion on days 1, 8, and 15 of a 28-day cycle.
Results: From March 1999 to October 2001, 20 patients were enrolled in the study. Ten (50%) had locally advanced disease; 7 (35%) had metastatic disease; and 3 (15%) had recurrent disease. Metastatic sites were liver (2 patients) and bone, lung, supraclavicular lymph nodes, liver and bone, and iliac and para-aortic lymph nodes (1 patient each). Among the 15 evaluable patients, 14 (93%) were male, and 11 (73%) had TCC. Nine patients (60%) had a WHO PS of 2. One patient had a complete response (CR) (7%), and 5 had partial responses (PRs) (33%) for an overall response rate of 40%; all responders had TCC. Five (33%) had stable disease, and 4 (27%) had progressive disease (PD). The only toxicities reported were grade 3 neutropenia in 3 patients (20%) and grade 3 anemia in 2 patients (13%). After a 1-year follow-up of the responders, the CR was maintained, and another 2 patients achieved CR (1 after cystoscopy and radiotherapy and 1 after a liver nodule assessment that was determined irrelevant to the disease). One patient maintained a PR, while 2 patients died of PD. After 2 years, 2 CRs and 1 PR (20%) remained.
Conclusion: In a multimodality approach, gemcitabine monotherapy can be used in patients with bilharzial-related bladder cancer of the TCC type who cannot tolerate platinum compounds or who have a poor performance status to achieve long-term, complete remission.

875 POSTER

Concurrent radiochemotherapy with Gemcitabine for locally advanced bladder cancer

A. Cringeanu, D. Stanculeanu, M. Savu, L.N. Minea, D. Mitulescu. *Institute of Oncology Bucharest, Bucharest, Romania*

Background: Combined chemo-radiotherapy may improve local control, organ preservation rate and long term survival in patients with locally advanced bladder cancer.
Gemcitabine shows certain activity in bladder cancer. Several studies confirmed that Gemcitabine have radiosensitizing properties. We proposed in this study to evaluate the efficacy and toxicity of the concurrent radiochemotherapy with Gemcitabine in locally advanced bladder cancer.
Material and methods: From March 2002 to May 2004 27 patients with locally advanced bladder cancer were enrolled onto this study. Patients characteristics: there were 21 male and 6 female, median age 53 years

(range 48–64), transitional cell carcinoma histologically confirmed, stage T3/T4, performance status ECOG 0–2. A chemo-radiotherapy regimen consisting of weekly gemcitabine (350 mg/m^2) with 45 Gy of external beam radiotherapy (1.8 Gy/fraction, 5 days/week) was delivered in five weeks on extended fields as appropriate and a boost on the bladder to a median total dose of 65 Gy. Patients were evaluated 4–6 weeks after combined treatment with cystoscopy and CT scans.
Results: 23 patients completed chemo-radiotherapy schedule. 4 patients interrupted the treatment, 3 because of grade 4 toxicity and 1 because of progressive disease. Clinical benefit was found in 19 of the 23 patients (7 complete response, 11 partial response and 1 stable disease). Progressive disease was found in the four remained patients. Adverse effects, especially haematological, were common but manageable. No chemoradiation-associated deaths were observed with this gemcitabine based regimen. Grade 3–4 haematological toxicity (neutropenia and/or trombocitopenia) occurred in 7 and 4 patients respectively. Grade 3 gastrointestinal toxicity (diarrhoea) occurred in 8 patients. Grade 3 cystitis occurred in 6 patients. Median follow-up period was 18 months; at this time 20 patients are still alive and 17 patients remain disease-free.
Conclusions: This schedule of Gemcitabine and radiation therapy is relatively well tolerated and has shown to provide prolonged clinical benefit response and disease stabilization in patients with locally advanced bladder carcinoma. These promising results should be further investigated.

876 POSTER

Combined treatment with Bicalutamide and ZD-1839 may be advisable in human prostate cancer in the early phases

M. Bologna[1], C. Festuccia[1], G.L. Gravina[2], P. Muzi[1], R. Pomante[3], L. Ventura[4], S. Speca[1], D. Millimaggi[1], A. Angelucci[2], C. Vicentini[2]. *[1]University of L'Aquila, Department Experimental Medicine and Basic Applied, L'Aquila, Italy; [2]University of L'Aquila, Department of Surgery, L'aquila, Italy; [3]G. Mazzini Hospital, Department of Pathology, Teramo, Italy; [4]S. Salvatore Hospital, Department of Pathology, L'Aquila, Italy*

Background: Combined treatment with Bicalutamide (Casodex) and ZD-1839 (Gefitinib, Iressa) in human Prostate Cancer (PCa) cell lines proved to be effective and hyperadditive (Festuccia et al., Int. J. Cancer, 2005). Relapses after androgen withdrawal in PCa are a significant cause of morbidity and mortality and pose the question of the ideal initial treatment of this very prevalent tumor.
Material and methods: We analyzed by immuno-histochemistry the expression of EGF receptor (EGFR), Erb-B2 (Her2) and PTEN (a tumor-suppressor) in a 50 patient cohort with localized tumors, treated by radical prostatectomy. Among these patients, 21 (group 1) received prostatectomy as initial treatment, whereas the other 29 (group 2) received neo-adjuvant androgen-ablation therapy for 3–6 months based on Casodex (150 mg/die) treatment before surgery. We also obtained primary cultures from 37/50 cases (17 of group 1 and 20 of group 2 patients) to test the Gefitinib antiproliferative/pro-apoptotic effects alone or in combination with Casodex.
Results: We observed a significant increase of EGFR and Her2 in tissues from group 2 patients. This indicates that EGFR/Her2 expression can be regulated in vivo by antiandrogens, as previously observed in cell lines. PTEN expression was lost after Casodex therapy. All PCa primary cultures were sensitive to both Gefitinib and Casodex (IC50 0.2 to 2.0 mM and 0.7 to >4.0 mM, respectively). We observed no differences between the IC50 values calculated in the two groups for Gefitinib indicating that increased EGFR expression was not a pre-requisite for effectiveness. In addition, Gefitinib (0.1 mM) increased the anti-tumour effects of Casodex of 10 fold and, Casodex (0.5 mM) increased the effects of Gefitinib of 2.5-fold. However correlating the IC50 values of single cases with the Her2 and PTEN expression we found that Her2 increase and PTEN decrease can be negative biomarkers of Gefitinib effectiveness.
Conclusions: Our findings favour the clinical development of combination therapies, by early association of Casodex and Gefitinib in newly diagnosed PCa patients by targeting simultaneously EGFR and AR in androgen-dependent/sensitive PCa, since the dual inhibition of AR and EGFR pathways could be useful in naive patients in order to extend the androgen-dependent phase and to delay the onset of EGFR-driven androgen-independence phase of PCa. 'Casodex', 'Gefitinib' and 'Iressa' are trademarks of the AstraZeneca group of companies.

877 POSTER

Apoptosis in urothelial bladder carcinomas and its relation to the expression of caspase 3 and apoptosis regulating proteins bax and bcl-2: prognostic implications

V. Theodoropoulos[1], A.C. Lazaris[2], I. Ghikonti[3], V. Tsoukala[4], E. Chamilos[1], G. Tamvakos[1], K. Aleksandrakis[1], I. Gerzelis[1], F. Sofras[5], I. Kastriotis[6]. *[1]Agia Olga General Hospital, Department of Urology, Athens, Greece; [2]School of Medicine, National and Kapodistrian University, Department of Pathology, Athens, Greece; [3]Agia Olga General Hospital, Department of Pathology, Athens, Greece; [4]School of Medicine, National and Kapodistrian University, Department of Pathology, Athens, Greece; [5]University General Hospital, Department of Urology, Heraklion, Greece; [6]Sismanoglio Hospital, School of Medicine, National and Kapodistrian University, Department of Urology, Athens, Greece*

Background: Apoptosis is the most significant component of programmed cell death that complements cell proliferation in maintaining normal tissue homeostasis. Bax protein accelerates apoptosis by antagonizing the apoptosis repressor bcl-2. Caspase 3 is the final step of the apoptosis-inducing protease pathway. We determined the association of apoptosis with the apoptosis related proteins bax, caspase 3 and bcl-2, as well as their interaction with prognosis in urothelial carcinoma (UC) of the urinary bladder.
Material and methods: Using immunochemistry we investigated the expression of bax, caspase-3 and bcl-2 in 88 primary UC bladder specimens. Apoptosis was detected by staining with a MoAb recognizing exposed single-stranded regions in the DNA of apoptotic cells (anti-ssDNA) and the apoptotic index (AI) was expressed as the percentage of the immunoreactive neoplastic nuclei. Kaplan-Meier survival curves were compared in order to define their possible prognostic role in disease-free survival (DFS).
Results: Positive staining for bax, caspase 3 and bcl-2 was noted in 50%, 90.8% and 55% of cases, respectively. Well differentiated UCs showed overexpression of bax and caspase 3 ($p < 0.05$), as well as a trend for strong expression of bcl-2 ($p > 0.05$). We noted a positive relation between bax and caspase 3 ($p < 0.05$), but no statistical association could be detected between the above proteins and bcl-2. AI increased with increasing grade and stage ($p < 0.05$), but was unrelated to the expression of the apoptosis related proteins. Log-rank test showed that high grade, T stage and increased AI had an adverse impact on DFS ($p < 0.05$), while patients with bax overexpression exhibited significantly longer DFS times ($p < 0.001$).
Conclusions: Apoptosis increases along with progression of the neoplastic lesions of the bladder epithelium. Although bax and bcl-2 are strongly expressed in urothelial bladder carcinomas, they don't seem to be the major regulators of apoptotic activity. The lack of relation of caspase 3 expression with degree of apoptosis may be due to the inability of immunohistochemistry to discriminate between the active and inactive forms of caspase. The adverse prognostic role of apoptotic rate is possibly the result of the loss of normal mechanisms controlling cell death, facilitating the survival of cells with increased ability to resist in unfavorable growth conditions. With regard to disease-free survival, Bax protein emerges as a promising favorable indicator.

878 POSTER

The expression of pentaspan membrane glycoprotein Prominin-1/CD133 is not limited to prostatic stem cells and is down-regulated in prostate cancer

E. Missol-Kolka[1], M. Haase[2], C. Liebers[1], S. Arl[1], C. Lorra[1], W.B. Huttner[1], D. Corbeil[3]. *[1]Max-Planck-Institute of Molecular Cell Biology and Genetics, Dresden, Germany; [2]Technical University of Dresden, Department of Pathology, Dresden, Germany; [3]Technical University of Dresden, Tissue Engineering Laboratories, BIOTEC, Dresden, Germany*

Background: Prominin-1 (CD133) is known as a cell surface marker of neural and hematopoietic stem/progenitor cells. One report has shown that Prominin-1 carrying the AC133 epitope can also be used to identify the prostatic basal stem cells (Richardson et al., J. Cell Sci. 2004, 117:3539). Furthermore, the expression of Prominin-1 is up-regulated in malignant hematopoietic diseases as well as in certain types of solid tumors such as those derived from the brain and kidney, which prompted us to evaluate whether Prominin-1 can be used as a prognostic and/or predictive clinical marker of prostate cancer.
Methods: The expression of Prominin-1 in normal adult human prostate as well as in 25 prostate cancer samples was monitored by immunohisto-chemistry.
Results: The analysis of human prostate revealed hE2, but not AC133, immunoreactivity on the apical side of prostatic epithelial cells whereas the AC133 immunoreactivity is restricted to a small population of cells