munochemotherapy is a new Treatment modality which can possibly improve local control as well as survival.

Methods: Analysed were the treatment results of 17 patients with symptomatic bone metastases from RCC, treated in the period from October 1995 to September 1998. All patients had further metastatic lesions outside the radiation fields. Radiotherapy was combined with immunochemotherapy using s.c. interleukin-2, s.c. interferon-alpha and i.v. 5-fluorouracil; the applied doses ranged between 40 and 55 Gy. The median follow-up is 12 months (range: 2 to 57 months).

Results: 2 patients achieved a complete remission (CR), 6 patients achieved a partial remission (PR) and 6 patients had stable disease (NC). Yet 4 patients died of the disease. The median tumor specific survival was 29 months (range: 13–98 months). 13 patients (80%) had a good analgetic response; from these, 4 had no pain after this therapy that has continued until today. The toxicity symptoms ranged between grade 1 and 3; there is no grade 4 toxicity according to WHO.

Conclusion: The combination of immunochemotherapy with local radiotherapy for symptomatic bone metastases is feasible and able to produce a good palliation with long lasting remission. No dose limiting toxicity were found.

1420 PUBLICATION

Urine GM-CSF as a prognostic factor of recurrence in bladder cancer (BC) patients, during intravesical treatment with BCG plus interferon A2b (BCG + IFN)

G. Kyriakou[1], V. Kapralos[2], T. Maousakas[1], C. Stravodimos[1], E. Serafetinidis[1], I. Castriotis[1], C. Constantinides[1]. [1]*Department of Urology, "Laikon" Hospital, University of Athens Medical School;* [2]*Department of Urology, "Ag. Olga" Hospital, Athens, Greece*

Purpose: This study was contacted to investigate whether the serial postoperative measurement of urine GM-CSF (uGM-CSF) in BC patients after BCG + IFN treatment can be correlated with the probability of relapse.

Methods: 50 pts with superficial BC stage T1GII and T1GIII entered in our study divided in two groups. Group A included 30 pts with recurrent disease and group B 20 pts at initial diagnosis of BC. The distribution of stages was similar in the two groups. In group A, BCG + IFN was performed after TUR of the tumor, while in group B no additional treatment was given. All pts were followed for at least two years, uGM-CSF was measured preoperatively and twice postoperatively (1st, 3rd month) in all patients using ELISA.

Results: The mean preoperative uGM-CSF levels did not differ significantly between group A and B. Although uGM-CSF levels decreased at the 1st postoperative month in both groups, these levels significantly increased at the 3rd postoperative month in group A ($p = 0.004$), while in group B remained low. 9 pts from group A and 7 from group B relapsed. All 9 relapsed group A pts had persistently low uGM-CSF postoperatively, while in the 21 remaining, uGM-CSF increased significantly between the 1st and 3rd month ($p < 0.01$). In all group B pts uGM-CSF remained low in both postoperative measurements irrespectively of relapse.

Conclusion: Intravesical treatment with BCG + IFN increases uGM-CSF levels presumably due to the induction of immunological response. Persistently low uGM-CSF seems to predict a higher probability of subsequent recurrence.

1421 PUBLICATION

Low grade transitional cell carcinoma of the bladder: Prognostic value of immunoreactivity for $p16^{ink4a}$, $p27^{kip1}$, pRb, p53, Ki-67 and bl2-10d1

L. Santos, T. Amaro, C. Jeronimo, M.J. Bento, P. Lopes, R. Carvalho, C. Lopes. *Portuguese Oncology Institute, Oporto, Portugal*

Purpose: The classic clinical-pathological variables have not allowed the identification of worst case prognosis. The Bl2-10D1 monoclonal antibody recognises a tumor-associated antigen is related with a more differentiated TCC. We evaluated the importance of immunoexpression of $p16^{ink4a}$, $p27^{kip1}$, pRb, p53, ki-67 and bl2-10d1 in the prognosis of low grade (Ta eT1) TCC.

Methods: The immunoreactivity for $p16^{ink4a}$, $p27^{kip1}$, pRb, p53, ki-67 and bl2-10d1 were evaluated in 68 primary low grade TCC treated consecutively at the Portuguese Oncology Institute of Oporto (IPO) between January 1989 and December 1993 and their first recurrences. The immunorreactivity obtained for each marker was compared with histological grade (WHO), Stage (UICC), Overall and disease free survival.

Results: The median follow-up was 56.4 months (1.9–99.9 months). In the primary tumors the percentage of cases with immunoreactivity for p53 was 42.6%. The absence of immunoreactivity was observed in following percentages: p16 (91.6%), p27 (1.3%) and pRb (19.2%). The percentage of cases with immunoreactivity for the Ki-67 protein (n^o of positive cells $\geq$ 20%/case) was 47.5%. The n^o of cases with immunoreactivity for the p53 cases was statistically higher in the recurrences than primary tumors ($p = 0.0001$). Concerning the other markers, no significant differences were observed. In relation to the grade and to stage we did not observe statistically significant differences among the studied markers. The disease free survival was significantly lower in tumors with Ki-67 immunoreactivity ($p = 0.008$) Additionally, the expression of Ki-67 was not associated with p53 accumulation or p16, p27 and pRb lack of immunoreactivity. The negative bl2-10d1 tumors had a statistically higher proliferation rate ($p = 0.04$).

Conclusion: The absence of immunoreactivity for p16, p27 and pRb did not correlate with prognosis. The accumulation of p53 protein was associated with tumor progression; however it was not related with a higher risk of recurrences. The Ki-67 imunoexpression was associated with a negative and significant correlation with disease free survival. The lack of immunoreactivity for bl2-10d1 in these tumors may be a marker of tumor aggressiveness.

1422 PUBLICATION

A phase I/II study of toxicity and response in patients receiving synchronous chemoradiotherapy for locally advanced bladder cancer (t2–t4) no/nx mo

S.A. Hussain[1], N.D. James[1]. [1]*CRC Institute for Cancer Studies, University Hospital, Birmingham, United Kingdom*

Purpose: This study was aimed to investigate possible synergy between radiotherapy and synchronous chemotherapy with 5-fluorouracil (5-FU) and mitomycin-C (MMC) in muscle invasive bladder cancer.

Method: Patients with T2–T4 No/Nx Mo muscle invasive bladder cancer were entered into this single centre study. Patients received 55 Gys of radiotherapy in twenty fractions over four weeks to the bladder with a margin of 15–20 mm. Concurrent chemotherapy was given with MMC 12 mg/m^2 on day 1 and 5-FU 500 mg/m^2 during week one and week four of radiotherapy treatment for five days on each occasion. The end points were bladder preservation, toxicity and local response rate.

Results: 20 patients have entered the study since March 1998. 2 patients were node positive. Median age was 68 (range 58–77) years, 14 male and 6 female, T2; 4 (20%), T3a; 4 (20%), T3b; 6 (30%), T4; 6 (30%), grade 2 TCC 6 (30%) and grade 3.14 (70%). 9 patients had hydronephrosis at presentation. Performance status was 2 in 1 case and 0–1 in the remaining 19. 9 patients received the chemotherapy treatment as an outpatient through a PICC line.

Haematological toxicity: 2 patients suffered from grade 3 and 3 from grade 2 thrombocytopenia; 5 patients had grade 2 leucopenia. 1 patient had grade 3 and 4 had grade 2 anaemia. Non-haematological toxicity: 1 patient had grade 2 renal toxicity. Grade 3 diarrhoea was encountered in 2 and grade 2 in 7 cases. 5 patients had grade 2 nausea. Symptomatic measures were sufficient to control non-haematological toxicity. Of the 12 (60%) patients due for 3 months response assessment so far, 2 (10%) patients had developed metastases. Of the remaining 10, 7 (70%) had a complete response (CR) and 3 (30%) had persistent disease on check cystoscopy.

Conclusion: Chemoradiotherapy is feasible in the management of elderly patients. The response is encouraging with acceptable toxicity.

1423 PUBLICATION

Surveillance and adjuvant chemotherapy in clinical stage I nonseminomatous testicular cancer (NSTC)

H. Onat[1], S.E. Bavbek[1], K. Uygun[1], M. Basaran[1], I. Kilicarslan[2], V. Uysal[2], F. Ozcan[3], M. Tunc[3]. [1]*Oncology Institute, Medical Oncology, Istanbul;* [2]*Istanbul Medical Faculty, Pathology Department, Istanbul;* [3]*Istanbul Medical Faculty, Urology Department, Istanbul, Turkey*

Sixty-seven patients (pts) with stage I NSTC seen between February 1991—August 1997 were retrospectively evaluated for prognostic factors, and results of surveillance/adjuvant chemotherapy (CT). Pts were staged after radical orchidectomy with chest, and abdomen computed tomography (ct), and tumor markers (alfafetoprotein-AFP, human chorionic gonadotropin-HCG). Stage I pts with elevated tumor markers were treated as stage II disease. Pts with stage I disease and adverse prognostic factors such as vascular invasion, choriocarcinoma component, spermatic cord invasion, or tunica albuginea invasion were given adjuvant CT. Median age was 28 (range: 18–64); 66 pts had radical inguinal orchidectomy. Four pts had a

history of orchiopexy. Tumor markers were elevated in 23 pts (34%) after surgery. The histology was combined germ cell tumor in 51 (76%); 20 pts (30%) had seminomatous and 15 (22%) choriocarcinoma components. Of the 44 pts with normal markers after surgery, 21 with no adverse prognostic factors were followed closely on a surveillance protocol. The follow-up included markers every month, chest x-ray every two months and abdomen ct every four months during the first year; markers and chest x-ray every two months and abdomen ct every six months on the second year; markers and chest x-ray every 3 months and abdomen ct every six months on the third year; and six-monthly visits thereafter to complete 5 years. Only one of the pts on surveillance (5%) relapsed and was treated with CT. Of 23 pts who received adjuvant CT (etoposide/cisplatin or bleomycin/etoposide/cisplatin) 2 had relapse. One of them died due to noncompliance, the other died very shortly after early development of massive liver metastases. Of the pts who received CT for elevated markers after surgery, 2 relapsed in the retroperitoneum; both were successfully salvaged by CT +/– retroperitoneal surgery. With a median follow-up of 46 months, median overall survival was 42 months, and the 5 year cumulative survival was 97%. Because of the very few number of events in this good-prognosis group, no difference in survival was detected between the surveillance and adjuvant CT groups. The survival data show that the patient selection for, and the policy of surveillance was justifiable. Randomized trials are needed for prognostic factor analysis in stage I NSTC.

1424 PUBLICATION

Chromosomal aberrations in bilharzial bladder cancer using fish technique

M. Khaled Hussein, M.S. Aly[1]. [1]*Cairo University (Beni-Suef Branch), Faculty of Science, Cairo, Egypt*

Cancer of the bladder is a frequent malignancy in Egypt and other developing countries in which bladder infection with the parasite Schistosoma haematobium is common. Several epidemiological, histopathological and clinical characteristics of cancer of the bilharzial bladder suggest that it is distinct from bladder cancer in other places in the world.

No numerical aberration of chromosomes that might be specific for bilharzial bladder carcinoma has so far been established. In this study, we used fluorescence in situ hybridization (FISH) with centromere-specific probes for chromosomes 1–12, 15–18, x and y to detect numerical aberrations of these chromosomes in frozen samples of 31 Egyptian patients affected with bilharzial carcinoma. The most common observed chromosomal imbalance was a loss of chromosome 9 (48.4%), with numerical aberration of chromosomes y and 17 being the second most frequent anomalies (22.2% and 19.4% respectively). The presence of such anomalies especially losses of chromosome 9 are associated with younger age group of patients as well as with lower grade tumor and negative pelvic node affection by the disease.

FISH analysis thus proved to be a useful method for detecting numerical aberrations of individual chromosomes, with application to touch print preparations of frozen – stored tissue having the advantage of exact sampling of cancer foci. This result also suggests that the mechanism of genetic progression of bladder cancer is independent of its etiology.

1425 PUBLICATION

Dose intensity (DI) and total dose (TD) of VAB-6 regimen for metastatic germ-cell tumours

S. Babović, S. Jelić, D. Radosavljević. *Institute for Oncology and Radiology of Serbia, Belgrade, Yugoslavia*

Purpose: We have analyzed DI and TD in VAB-6 regimen with respect to tumour response and survival.

Patients and Methods: The retrospective study was performed on 70 metastatic germ-cell tumour patients (pts). Pts were given up to six courses of modified VAB-6 as the primary regimen (vinblastin 10 mg, actinomycin D 2 mg, cyclophosphamide 1000 mg D1, bleomycin 10 mg D1–6, cisplatin 50 mg D 7–10).

Results: The complete remission was achieved in 51/71 pts (73%). The overall 5-year survival rate was 68%, and 10-year survival rate was 64%. The average relative dose intensity (ARDI) of planned regimen was 0.75 of standard one. ARDI of applied regimen was 0.90 of planned VAB-6 regimen. The mean value of relative DI (RDI) for cisplatin was 0.88. Average TD/TD of standard regimen ratio for cisplatin was 1.77.

Comparing groups of pts received RDI $\geq$ 0.8 and RDI < 0.8 (for each drug, and for the regimen as a whole), no significant differences were noticed in terms of efficacy and survival.

Conclusion: Two third of pts who are alive 10 years after treatment with greater total dose of cisplatin received permit speculation that TD of cisplatin might influence more the regimen efficacy than ARDI.

1426 PUBLICATION

Gemcitabine (G) and vinorelbine (V) in pretreated or elderly transitional cell carcinoma (TCC) patients (PTS): A phase II study

F. Ferrau[1], R. Bordonaro[1], R. Aiello[1], S. Cordio[1], M. Failla[2], D. Giuffrida[1], G. Lavenia[1], A. Pappalardo[1], D. Priolo[1], G. Failla[1]. [1]*S. Luigi Hospital, Division of Medical Oncology, Catania;* [2]*S. Luigi Hospital, Biologist, Catania, Italy*

The aim of the study was to verify tolerability and efficacy of G and V combination in TCC pts relapsed after platinum-containing regimens (5 pts) or not amenable to platinum because of age > 70 years or poor performance score (5 pts). Mean age was 68.5 (51–78), M/F ratio 2/10; sites of metastases were lung (3 pts), lung and nodes (2), liver and lung (2), pelvis nodes and bone (1); 1 pt had synchronous kidney and lung metastases, 1 pt had locally advanced TCC. 5/10 were platinum pretreated. Mean disease free interval was 8 months (5–45). G (1000 mg/mq/d) and V (25 mg/mw/d) were given on day 1 and 8, every three weeks; no elective g-csf was used. All pts are evaluable for toxicity and response. Fortythree cycles were administered, with a mean number of 4.3 cycle/pt. Grade III–IV toxicities occurred in 1 pt (G IV emesis plus G III neutropenia in a 73 year old women at the 5th cycle, after cPR); other toxicities were G II emesis (5 cases), G I fever (3), AST/ALT elevation (2), cutaneous rush (1). Responses were complete in 2 pts (1 in lung and liver, 8 months duration; 1 in lung, 8+ months); partial in 5 (mean duration 6+ months); 2 stable disease, 1 progression (liver). This treatment seems feasible and active; further studies with larger number of patients are needed.

1427 PUBLICATION

Value of humoral immunity, angiogenesis and basement membrane changes in the prediction and prognosis of bladder carcinoma

S. Mansy[1], H. Yehia[1], A. Ismail[2], W. Tosson[2]. [1]*TBRI, Electron Microscopy (Pathology), Giza;* [2]*TBRI, Urology, Giza, Egypt*

Purpose: The aim of this work was to assess the value of immunoglobulin secreting cells (mediators of humoral immunity), angiogenesis and basement membrane changes in the prediction and prognosis of neoplastic bladder lesions.

Methods: 23 specimens (sp.) of TCC stage pTa, pTis, pT1, 39 sp. of non malignant urothelial abnormalities with atypia either with mild, moderate (26 sp.) or severe (13 sp.) atypia and 7 normal control sp. were subjected to direct immunofluorescence technique using antihuman polyvalent Ig. Positive cells were scored/HPF. Also the sp. were processed for ultrastructural study.

Results: Although a significant increase in the number of Ig secreting cells was elicited in neoplastic and dysplastic bladder lesions versus the benign lesions with mild or moderate atypia ($P < 0.01$), yet no significant difference was detected between the different grades or stages of the studied TCC or between them and the severe dysplastic lesions. On the other hand, the appearance and the increase in the number of abnormally thickened and chained microvasculature just beneath the urothelial BM correlated with the severity of BM involvement in severe atypia and tumor lesions as detected by electron microscopy.

Conclusion: Apart from the detected prognostic value of ultrastructural changes seen in BM of tumor lesions, the appearance of abnormal microvasculature with the occurrence of small vacuoles or irregular thinning in the BM and increase in Ig secreting cells in severe dysplastic lesions may be a predictor factor for a malignant behaviour.

1428 PUBLICATION

Contribution to split-course method in radiotherapeutic treatment for bladder cancer

M. Erak[1], J. Babic[1], Z. Kuzmanovic[1], D. Erak[1]. [1]*Instiitute of oncology Sremska Kamenica, Radiotherapy, Sremska Kamenica, Yugoslavia*

Background: Bladder carcinoma is a rare carcinoma relatively, about 5% malign tumor in males and 3% in females. It has been most frequent in the seventh and eighth life decades. In the last decades an increased number