Methods: Twenty-five evaluable HRPC pts with Karnofsky PS ≥ 60% received CTX: 100 mg/m^2/day × 10 every 3 weeks. Evaluation criteria of response: serum PSA and measurable disease. Median pre-CTX PSA level: 42.6 ng/ml (range: 0.6–761.0 ng/ml); 3 pts had normal PSA. Age range: 54–87 years (median: 73 yrs).

Results: With a median follow-up of 10 months (mo), range: 2–31 mo, we obtained 5 (20.0%) complete remissions (CR) with a median duration of 15 mo (range: 5–22 mo); 5 (20.0%) partial remissions (PR) lasting 3 to 20 mo (median: 6 mo); 5 (20.0%) stable diseases (SD), with a median duration of 6 mo (range: 1–7 mo) and 10 (40.0%) progressions (P). Median overall survivals after initiation of CTX were: CR: 27 mo (range: 6–31 mo); PR: 13 mo (range: 4–29 mo); SD: 8 mo (range: 3–16 mo); P: 9 mo (range: 2–15 mo). There were no deaths among CR, PR, and SD pts; 60.0% of P pts died of active HRPC. Number of CTX cycles to achieve objective response (CR + PR): 5 (range: 1–15). Toxicity was mild and well tolerable. (To be presented).

Conclusions: CTX is an efficacious and well tolerated treatment for HRPC pts. This may reflect in an apparent improvement of survival and quality of live of objective responders.

1415 PUBLICATION

The accuracy of patient positioning in irradiation of prostate cancer by portal film analysis

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Purpose: Portal imaging is used for quality assurance of radiotherapy treatment fields. We analyzed retrospectively the accuracy of treatment delivery in 34 prostate cancer patients (pts) treated by 4 field technique (BOX) pelvic irradiation followed by boost arc therapy, and in 25 pts treated by 4 "small" pelvic fields.

Methods: We compared weekly portal images to digitized simulation films using a computer assisted quality assurance program (PIPSpro, Masthead Canada) using fiducial points and contrast improvement filters technique to determine overdose and underdose of each portal film.

Results: Pelvic fields portal films of 34 pts (194, 97 AP-PA, and 97 lateral) were analyzed. The mean equivalent square field size was 16 × 16 cm^2 in AP-PA and 14.2 × 14.2 cm^2 in lateral. The average overdose area (AOA) was 2.75% (range 0.08–14.05), and average underdose area (AUA) was 2.74% (range 0.03–23.92) in AP-PA portals. In the lateral portals it was 2.49% (range 0.21–16.03), and 2.78% (range 0.29–29.55) respectively. Portal films of 25 pts (194, 98 AP-PA, and 96 lateral) treated by small fields were analyzed. The mean equivalent square field size was 10.6 × 10.6 cm^2 in AP-PA and 10.3 × 10.3 cm^2 in lateral. The AOA was 0.88% (range 0.00 × 2.80), and AUA 0.86% (range 0.00–2.70) in AP-PA portals, 1.03% (range 0.10–3.80), and 0.82% (range 0.00–2.40) in lateral portals.

Conclusion: The accuracy of prostate cancer patient positioning in our institution is in the range of 25% for large fields, and 1.0% for small fields.

1416 PUBLICATION

Rational mutagenesis of a recombinant anti-tumour antibody

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Purpose: C595 monoclonal antibody (an anti-MUC1 mucin antibody) and its fragments are currently being used to image superficial bladder tumours. To promote greater understanding of how C595 interacts with MUC1, molecular modelling, site-directed mutagenesis and standard immunoassays have been utilised to probe the antigen binding pocket

Methods: A model of C595 variable fragment (Fv) was produced using homology modelling. Residues of suspected importance in antigen recognition were selected for mutagenesis. Oligonucleotide directed mutagenesis was employed to produce mutations, and mutants were expressed in E. coli. ELISAs were performed to analyse effects of mutations on association and dissociation to MUC1.

Results: Ten mutant Fvs have been produced, each with differing relative affinities for MUC1. Mutations of Asp to Asn within the pocket yielded much longer association rates (H97DN, H100DN & H95DN have 22%, 64% and 87% of parental Fv association rate respectively), while a mutation of Asn to Asp in the pocket gave a longer relative dissociation rate (L93ND – 24% increase on parental rate). Some mutations had no appreciable effect on the antibody-antigen interaction.

Conclusion: Molecular modelling coupled with site-directed mutagenesis of an antibody binding pocket is a powerful tool for examining the antibody/antigen interaction. This study has scrutinised the antibody pocket for important residues involved in the interaction with MUC1 and has provided new lead entities for use as radio-imaging/-therapy agents in bladder cancer.

1417 PUBLICATION

Radiation therapy for Peyronie's disease

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Purpose: To retrospectively analyse treatment outcome in patients (pts) irradiated for Peyronie's disease (PD).

Methods: The radiotherapy (RT) records of pts irradiated for PD between 1982 and 1997 were reviewed. The RT schedule consisted of 13.5 Gy (9 × 1.5 Gy, 3 fractions per week) using orthovoltage in 138 pts, or 12 Gy (6 × 2 Gy, daily fractions) using electrons in 39 pts. RT schedule was not clearly reported in 2 pts.

Results: Of the 179 pts (median age 52 years), 78% presented with painful erections and 89% with penile deformity. The symptoms were present for a median duration of 6 months (range 1–72 months) prior to RT. 17% of pts had been previously treated (unsuccesfully) with other methods. Fibrous plaques were dorsally localized in 95% of pts and had an average surface of 3.3 cm^2 (range 0.5–18 cm^2). No RT related complications were reported except for transient dysuria in a single pt. Of the 139 pts who attended follow-up at a mean of 3 months (range 0–13 months), 71% reported that their pain was diminished or had disappeared. 21% of pts reported a decrease in their penile deformity. From a questionnaire mailed to 139 pts it was found that 72% were sexually active, 48% complained of erectile dysfunction and 49% were dissatisfied with their current sex life.

Conclusion: Low dose external RT (12–13.5 Gy) appears to be an effective treatment in pts with PD who have persistent complaints of painful erections. No significant RT associated morbidity is seen with such doses.

1418 PUBLICATION

Detection of bladder cancer by qualitative determination of human complement factor H-related protein (hCFHrp) in urine

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The purpose of this study was to assess a new qualitative urinary tumor marker for transitional cell carcinoma of the urinary bladder (TCC), human complement factor related protein (hCFHrp).

Urine samples of 298 individuals were examined for the presence of the human complement component H related protein (hCFHrp), using the BTA STAT test. The control group included 76 healthy volunteers and 110 patients with benign urologic diseases. The study group consisted of 82 patients with histologically proven bladder cancer. Samples of all patients were obtained prior to therapy.

HCFHrp was positive in 66/82 samples of patients with histologically proven bladder cancer (sensitivity: 80.5%). Sensitivity was dependent on tumor stage (pTa: 36.4%, pT1: 92.9%, pT2: 94.1%, pT3: 100%, pT4:100%). All patients with pT1G3 tumors were identified by the test. HCFHrp was negative in all healthy individuals (specificity 100%). In contrast, 58/110 HCFHrp determinations in patients with benign urologic disorders were false positive, resulting in an overall specificity of 72%.

We therefore conclude that hCFHrp is a sensitive marker for detection of bladder cancer and for identification of patients at high risk. BTA STAT is thus potentially useful for follow-up-studies in patients in whom benign disorders of the urinary tract can be excluded.

1419 PUBLICATION

Metastatic renal cell carcinoma: A new approach with combined radioimmunochemotherapy

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Purpose: Patients with secondary bone metastases from renal cell carcinoma (RCC) have a poor prognosis. The presented radioim-

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)

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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

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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° of positive cells $\geq$ 20%/case) was 47.5%. The n° 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

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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)

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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