

munotherapy 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 immunotherapy 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 immunotherapy 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.

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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 post-operative 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.

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PUBLICATION

Low grade transitional cell carcinoma of the bladder: Prognostic value of immunoreactivity for p16^{ink4a}, p27^{kip1}, pRb, p53, Ki-67 and b12-10d1

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Purpose: The classic clinical-pathological variables have not allowed the identification of worst case prognosis. The B12-10D1 monoclonal antibody recognises a tumor-associated antigen is related with a more differentiated TCC. We evaluated the importance of immunoreactivity of p16^{ink4a}, p27^{kip1}, pRb, p53, ki-67 and b12-10d1 in the prognosis of low grade (Ta e T1) TCC.

Methods: The immunoreactivity for p16^{ink4a}, p27^{kip1}, pRb, p53, ki-67 and b12-10d1 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 immunoreactivity 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 b12-10d1 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 immunoreactivity was associated with a negative and significant correlation with disease free survival. The lack of immunoreactivity for b12-10d1 in these tumors may be a marker of tumor aggressiveness.

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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/m² on day 1 and 5-FU 500 mg/m² 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.

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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 (alpha-fetoprotein-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