2, was also associated with increase pretreatment PSA serum levels (>4ng/ml) (p<0.001). The distribution of p53 and bcl-2 expression, in prostate carcinomas, was statistically significant for stages T2a and T2b (p<0.001). On the contrary, no significance for T2c and T3a (p:0.24 for p53 and p:0.61 for bcl-2) was found as for as the histological stage. P53 and bcl-2 proteins had significant prognostic value for the disease free survival, remained an independent prognostic marker by Cox multivariate regression analysis.

Conclusions: The expression of p53 and bcl-2 appears to be an additional significant marker in the field of prognosis and outcome of patients with prostatic adenocarcinoma.

897 POSTER

High-dose ibandronate is effective and well tolerated in the treatment of pain and hypercalcaemia due to metastatic urologic cancer

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Introduction and objectives: Up to 20% of all urological malignancies are complicated by paraneoplastic hypercalcemia due to increased bone resorption and enhanced renal tubular reabsorption. Increased bone resorption is associated with osteolytic bone metastases and severe bone pain in metastatic renal cell and bladder cancer. Bone pain, reduced mobility and decreased quality of life due to osteoblastic metastases still represent a therapeutic dilemma in hormone refractory prostate cancer. Ibandronate is a third generation bisphosphonate with a high analgesic potency and a calcium lowering effect. We undertook a prospective pilot study to evaluate the safety and tolerability of high dose ibandronate in metastatic urological cancer.

Patients and methods: 59 patients (n=45 prostate cancer, n=9 renal cancer, n=5 bladder cancer) with hypercalcemia (n=6, group A) or painful osseous metastases (n=53, group B) were included in the prospective study. All patients had a serum creatinine level greater than 2 mg/dl. Patients in group A also had serum calcium levels greater than 2.8 mmol/l, while patients in group B had a mean pain score of 6.8 using a VAS from 110. In group A, after fluid repletion, ibandronate 6mg i.v. in 500ml glucose 5% was infused over 1 hour and repeated daily until serum calcium levels had normalized (median three infusions, range 25). In group B, ibandronate 6mg was given i.v. for three consecutive days, and continued at 4-week intervals.

Results: In group A, s erum calcium values fell progressively from day 2, reaching a nadir on day 4, and normocalcemia was maintained for 28 days. In group B, bone pain was significantly improved in 44/53 (83%) of the patients, starting on day 2; the mean pain score on day 3 was 2.5 (p<0.001). None of the patients in groups A or B demonstrated an increase in serum creatinine or serum urea nitrogen concentrations. Besides a slight decrease in serum calcium concentrations in 7/59 patients (12%), no alterations in laboratory measures were detected. Eight patients (14%) from groups A and B developed fever and flu-like symptoms as the only therapy-associated side effects. No renal adverse events were reported.

Conclusions: Application of high dose ibandronate results in a significant and fast normalization of serum calcium levels in patients with paraneoplastic hypercalcemia and a significant pain relieving effect in 83% of patients with painful osseous metastases. Despite the intensive dosing schedules of i.v. ibandronate in this study, we did not encounter renal toxicity or any other significant therapy-associated side effects.

898 POSTER

Chemotherapy induced peripheral neuropathy in testicular cancer patients treated with cisplatin,etoposide and bleomycin(PEB)

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Purpose: Evaluation neurological late toxicity in testicular cancer patients (pts) treated with PEB (cisplatin,etoposide and bleomycin) combination chemotherapy (CHT).

Methods: From January l997 to January 2002, 48pts with testicular cancer, were treated in hospital with PEB combination chemotherapy, after orchiectomy received at least 3 cycles of CHT. Median age was 32 (18-64). Were followed for at least 1 year after CHT and retrospectively evaluated for neurotoxicity. All pts had EMG (electromyography) and physical examination by a neurologist.

Results: Only 4 pts had pathological findings of EMG (axonal neuropathy). 8 pts had symptoms with paresthesias at distal extremities, 2 pts have grade I neurological toxicity according to the WHO toxicity scoring system.

Conclusion: We concluded the combination PEB CHT is safe, well tolerated and treatment with 3 cycles did not lead no clinically significant neuropathy.

899 POSTER

Indirubin, the active constituent of a Chinese antileukaemia medicine induces growth arrest and apoptosis in renal cell cancer cells.

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Indirubin is the active ingredient of Danggui Longhui Wan, a mixture of plants that is used in traditional Chinese medicine to treat chronic diseases. The cell permeable Indirubin-3'-monoxime is a selective and potent inhibitor of cyclin-dependent kinases (CDK) and was shown to be active in several hematological tumor models. In this study we investigated if Indirubin-3'-monoxime (Alexis Inc.) can induce apoptosis and tumor cell death in four different, one animal (Renca) and three human (A498, Caki 1, Caki 2), renal cell cancer cell lines. The growth inhibitory properties were evaluated by EZ4U, a cytotoxic assay; whereas induction of apoptosis was determined by flowcytometry of Annexin-V/PI staining during treatment. Further, we investigated a potential synergism of a combined application of Indirubin with Paclitaxel, as this drug targets the mitotic spindle and cell cycle regulation, too. The efficacy of Indirubin-3'-monoxime yielded different results in the cell lines. In Renca, A498 and Caki-1 we found a significant dose and time related, but reversible growth arrest, though not apoptosis. When combined with Paclitaxel, a significant amount of apoptosis was induced, which was higher then with Paclitaxel treatment alone, suggesting that there might be a synergistic effect for the induction of apoptosis. A synergistic effect of a combination of Indirubin-3'-monoxime and Paclitaxel was shown in two cell lines (A 498, Caki-1). In Caki-2, a highly malignant cell line, growth inhibitory efficacy was limited, all three applications (Indirubin-3'-monoxime, Paclitaxel, combination) induced only a minor amount of apoptosis. In summary, Indirubin-3'-monoxime seems a promising candidate for a molecular targeted approach in renal cell cancer therapy. However, its actions alone and with other agents need further evaluation.

900 POSTER

Adjuvant chemotherapy(CHTH) in patients with high-risk urothelial cancer of urinary tract.

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Background: The role of adjuvant CHTH in high-risk urothelial cancer pts is disputable. Adverse prognostic factors are not fully determined.

Objective: the retrospective evaluation of results of adjuvant CHTH in patients (pts) with urothelial cancer of urinary tract after radical surgery.

Patients and methods: From 1994 through 2002 136 pts with urothelial cancer of urinary tract and no residual macroscopic disease following radical surgery with high-risk features for relapse (defined as: grade 3, positive lymphonodes, vascular/lymphatic invasion) received 2 (to 1996) or 3 (to 2001) or 4 cycles of adjuvant CHTH. Median age was 60 (41-76), male/female ratio 115/21. All pts had undergone macroscopically radical operation (7-nephroureterectomies, 3- partial cystectomies, 123-radical cystectomies/cystoprostatectomies). The local status was: pT2-25pts, pT3-87, pT4-24. The nodal status was: pN0-60 pts, pN1-29,pN2-30,pN3-2, in 15 pts the pN status wasn't determined. For 81 pts the median number of excised lymphonodes was 4 (1,30). 40 pts had G2, 96- G3. Vascular/lymphatic vessel invasion was present in 74 of 80 pts in whom this feature was defined. 134 pts received MVC (metotrexate, vinblastine, cisplatin), 2 pts MVCarbo. 9 pts received 1 cycle of CHTH (in 8 cases CHTH was stopped because of toxicity, 1 pt resign of CHTH), 26- 2 cycles, 94- 3 cycles, 6- 4 cycles, 1- 5 cycles.

Results: 54/136 pts (39.7%) are alive with no evidence of disease, 23/136 (16.9%) are alive with PD, 58/136 (42.6%) died of disease. 66/136 (48.5%) relapsed with the median TTP 11.8 mos (2.7-72). The median OS is 17.9 mos (0.6-101).