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).

Conclusions: Adjuvant CHTH in urothelial cancer of urinary tract isn't a standard treatment. Half of pts treated with adjuvant CHTH relapsed in one year. The risk of relapse remained comparable with results obtained in pts without adjuvant treatment. The optimal strategy of management in this high-risk pts is to be defined in prospective way.

901 POSTER

Effective first-line chemotherapy with docetaxel and gemcitabine in advanced bladder cancer (ABC)

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Background: Docetaxel and gemcitabine are two promising drugs in ABC, yielding high response rates as monotherapy with manageable toxicity. Moreover, there is evidence of synergism between docetaxel and gemcitabine in various tumours.

Materials and methods: Twenty-one patients (16 male, 5 female) with stage IV ABC have been enrolled. Aged 42-73 (median 63) years, ECOG PS 0-2, 6 and 7 patients had been treated with adjuvant chemotherapy and radiotherapy, respectively. Treatment consisted of docetaxel 75 mg/m^2 d1 as a 60-min iv infusion after standard premedication and gemcitabine 1000 mg/m^2 dl + d8 as a 30-min iv infusion, repeated every 3 weeks for up to 6 cycles.

Results: A total of 105 cycles have been administered (median 5/patient). Grade 3-4 haematological toxicities included neutropenia 20%, thrombocytopenia 10%, and anaemia 10%, with febrile neutropenia in 4 patients and 9 cycles. G-CSF and EPO were judged necessary in 11 and 5 patients, respectively. Treatment delay was required in 5 patients and 7 cycles. No toxic deaths occurred. Haematological toxicity was generally manageable and as seen in other studies with the two agents (alopecia, asthenia, serious onycholysis, diarrhoea, mucositis, dyspnoea). Thirteen patients responded clinically and/or radiologically with 3 complete responses (2 liver metastases); 5 patients had stable disease. Median time to progression exceeds 6 months.

Conclusion: Preliminary results suggest that the docetaxel-gemcitabine combination is effective and well tolerated in ABC. The study is ongoing.

902 POSTER

Nonseminomatous germ cell testicular tumors clinical stage I: a retrospective analysis.

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The cure rate for nonseminomatous germ cell testicular tumors (NSGCTT) clinical stage I is very high (99%). This can be achieved by different therapeutic strategies. We analyzed retrospectively 100 patients (pts) followed by 2 institutions: 42 accepted and entered into a surveillance program (SP), 58 were treated with retroperitoneal lymph node dissection (RPLND). Patients had either normal serum markers or declining at half-life. Patients characteristics were: median age 28 years (range 16-71) for SP and 28 (range 17-54) for RPLND; embryonal carcinoma component was predominant in 72.5% (SP) and 56% (RPLND pts); vascular invasion was present in 21.4% (SP) and 25% (RPLND pts); serum tumor markers were elevated in 74% (SP) and 47% (RPLND) of cases before orchiectomy; pathological stage II, after RPLND, were revealed in 7 pts. Median follow-up was 9.8 years (9- 250 months) for SP and 8.3 (15-323 months) for RPLND respectively. Relapses were as follow: 14 (33.3%) for SP and 8 (14%) for RPLND; all were treated with cisplatin-based chemotherapy and surgery of residual masses. In the first group sites of relapses were: retroperitoneum (6 pts), lung (2), retroperitoneum and lung (1), mediastinal and retroperitoneal lymph nodes (1); four pts had only an increase of serum tumor markers. Relapses after RPLND were: lung (3), retroperitoneum (2), inguinal lymph nodes (1), retroperitoneum and lung (1), lung retroperitoneal and mediastinal lymph nodes (1). Median time to relapse (TTR) was 6 months (range 2-19) for SP and 4 (2-19) for RPLND. None of the prognostic factors studied (age, tumor size, pathological stage, histology, vascular invasion and serum tumor markers) was predictive of relapse, neither for SP nor for RPLND. In each group the disease specific survival was 100%: one patient died for HIV-related causes in the SP group, and one patient died for car accident 3 years after RPLND. There is only one patient, followed initially with the SP, alive with disease.

Conclusions: i) both strategies allow an optimal cure rate; ii) in each group relapses were observed; iii) median TTR was similar; iv) no prognostic factor examined was predictive of relapse. Therefore, independently from the strategy, an accurate follow-up must be performed for the first 2 years and the patient's choice should be a fundamental point in the decision making.

903 POSTER

Capecitabine-monotherapy and in combination with immunotherapy in the treatment of metastatic renal cell carcinoma

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Purpose: Capecitabine is a novel fluoropyrimidine carbamate, orally administered and selectively activated to fluorouracil by a sequential triple enzyme pathway in liver and tumor cells. This prospective trial aimed to evaluate the therapeutic effects and systemic toxicities of capecitabine monotherapy and capecitabine treatment combined with biological response modifiers in patients with metastatic renal cell carcinoma.

Patients and Methods: 54 patients suffering from metastatic renal cell carcinoma progressing under first-, second-, or third-line treatment entered the trial. Capecitabine was given orally at a dose of 2500 mg/m^2 daily divided into two doses for 14 days, followed by seven days' rest in the monotherapy as well as in the combination treatment. This schedule was repeated in three-week cycles. The combination therapy consisted of capecitabine and an immunotherapy treatment, which consisted either of interferon-gamma 1b (100 mg/d) administered consecutively five times weekly during weeks 1 and 2 and recombinant interleukin-2 (4.5 MU/d) administered on 4 consecutive days during weeks 3 and 4, every 6 weeks, or alpha-interferon (6 MioIE/d) administered three times a week.

Results: 52 patients are now evaluable for response and 54 patients for toxicity. We observed a partial response to treatment in 5 patients (9.6%), minor response in 5 patients (9.6%), stable disease in 32 patients (61.6%), and only 10 patients (19.2%) showed continued disease progression despite treatment. Outpatient capecitabine was well tolerated. We did not observe any WHO-grade IV toxicities.

Conclusion: Capecitabine monotherapy and capecitabine treatment in combination with biological response modifiers appear to be effective regimens with favourable toxicity profiles in patients with advanced renal cell carcinoma. Capecitabine monotherapy seems to be superior than the combination treatment because of its easier application form.

Symptom management/Quality of life

904 POSTER

Health-related quality of life in randomised controlled trials in colorectal cancer.

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Health related quality of life (HRQOL) is an important outcome in clinical trials in colorectal cancer yet there is no established consensus on the methods of optimal measurement of HRQOL for these patients. Recent publications have raised questions regarding the quality of some published health-related quality of life (HRQOL) assessment studies in cancer clinical trials. Hence, t he aim of this systematic review was to evaluate levels of reporting of HRQOL in randomized trials in colorectal cancer.

A comprehensive search from 1980 to March 2003 was performed to identify randomised controlled trials (RCTs) of colorectal cancer patients who had undergone a HRQOL assessment. Articles were identified mainly by MedLine, CancerLit, and the Cochrane Library. All studies enrolling at least 50 patients and using a HRQOL patient self-reported measure were included. Two reviewers (FE & AB), according to a pre-defined-coding scheme, independently extracted the data and assessed all trials to consistently evaluate their methodological quality.

A total of 34 RCTs enrolling 10,180 colorectal cancer patients were identified. The majority of the studies (74%) examined metastatic patients. 26% of the RCTs examined HRQOL as a primary endpoint. Different HRQOL measures were used to assess outcomes, with the EORTC QLQ-C30 being the most common measure used (47%). The remaining trials used different