5b the best sensitivity (71%) and specificity (96%) was seen with the cut-off point = 4.98 U/L, and for MMP-9 the best sensitivity (43%) and specificity (82%) with the cut-off point = 96.1 ng/ml. Patients with TRACP 5b ($p = 0.002$) or tALP ($p < 0.001$) levels above determined cut-off values showed significantly shorter survival than patients with low marker levels. MMP-2 and MMP-9 were not associated with survival.
Conclusions: TRACP5b is a novel marker of skeletal metastases and a predictor for survival in advanced PC.

861 POSTER

Retrospective study of inhaled IL-2 as treatment of lung metastasis of renal cell carcinoma. Spanish and Portuguese experience

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Background: Systemic IL-2 has been used for the last decade to treat metastatic renal cell carcinoma (MRCC). Locoregional administration of this cytokine could improve the risk/ benefit ratio of this drug. The objective of this study was to obtain efficacy and safety data on inhaled rIL-2 used in clinical practice in lung metastatic renal cell carcinoma (LMRCC) patients.
Material and Methods: The study was designed as a retrospective chart review in LMRCC patients being treated with inhaled rIL-2. Between September 2000 and April 2005, 32 centres in Spain and 3 in Portugal provided data from 80 LMRCC patients treated with inhaled IL-2. The treatment schedule was: 3 cycles of 36 MIU rIL-2 per day for 5 days/week for 12 weeks (with one week treatment free between cycles) in Spain and for 3 weeks (out of each 4 weeks) for 12 weeks in Portugal. Efficacy was assessed by best response following each treatment cycle and overall. PFS and OS were measured from the time of administration of the first dose of inhaled rIL-2 until progression, last follow up date or death, respectively The Kaplan-Meier method was used to estimate progression free survival (PFS) and overall survival (OS). Safety data were analysed using descriptive statistics, with toxicities expressed as number of toxicity reported weeks, describing grade and cycle.
Results: A total of 1290 treatment weeks were studied. Cough was the most frequent adverse event (reported in 27.8% treatment weeks), tending to be less frequent after the first 12 weeks of treatment. The majority of adverse events were reported to be only grade 1 or 2 in severity. Response rates after 12 weeks treatment were: 2 (2.7%) Complete Response; 10 (13.6%) Partial Response; 21 (28.7%) Stable Disease. At the present moment there were only 48 patients' data for survival calculations. Median PFS and OS were 4.5 (range 0.5–17.3) and 10.7 (range 0.4–42.9) months. At least 10 patients (20.8%) were alive for further than 24 months.
Conclusions: These initial results confirm that IL-2 locoregional administration in LMRCC can improve the risk/ benefit ratio of this drug compared to systemic therapy, maintaining its efficacy with an outstanding toxicity reduction.

862 POSTER

Biochemical response to neoadjuvant hormonoterapy may predict biochemical control rate and distant metastasis free survival after total short term androgen deprivation and conformal radiotherapy in the treatment of prostate adenocarcinoma

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Background: We assessed the prognostic factors affecting survival after short term total androgen deprivation (TAD) and radiotherapy in the treatment of localized prostate cancer.
Materials and Method: One hundred twenty-eight patients with T2-T3N0M0 prostate adenocarcinoma patients were treated. Stage T3, PSA $\geqslant$10 ng/dL and Gleason Score (GS) 7 and above were considered as high risk criteria and in case of positivity in one of them the patient was considered as high risk, otherwise treated as low risk. All patients were prescribed neoadjuvant TAD before radiotherapy. In high risk patients, TAD was continued for 6 months after completion of radiotherapy. Total radiotherapy dose was 73.6 Gy at ICRU reference point.
Results: Median follow-up was 48 months. Nineteen patients were in the low and 109 were in the high risk group. Five-year cause specific survival, biochemical control rate (bCR), and distant metastasis free survival rate were 94%, 80%, and 87% respectively. bCR was 87% for patients with PSA $\leqslant$1 ng/dL after 3 months neoadjuvant TAD, and 69% for patients with PSA >1 ng/dL after 3 months neoadjuvant TAD. Multivariate analysis showed that pre-radiotherapy PSA level measured after 3 months neoadjuvant TAD, age and T stage were significant prognostic factors determining bCR, and distant metastasis-free survival.
Conclusions: Response to neoadjuvant TAD may predict biochemical failure and distant metastasis free survival in patients with prostate carcinoma receiving conformal radiotherapy.

863 POSTER

A phase II study of BAY 43–9006 (sorafenib) in patients with androgen-independent prostate cancer (AIPC)

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Background: BAY 43–9006 (sorafenib) is a bis-aryl urea and a potent inhibitor of b – and c – Raf kinase, PDGFR and VEGFR-2. Accumulating evidence suggests that the Ras-Raf-MAPK-ERK signaling pathway is dysregulated in the setting of AIPC. Furthermore, published studies have shown a role for anti-angiogenic therapy for AIPC. We have launched a phase II study to determine the clinical and biological activity of BAY 43–9006 in patients with AIPC.
Methods: Patients are enrolled in an open-label, single arm phase II study. The primary objective is to determine if BAY 43–9006 is associated with a 50% 4 month probability of progression free survival as determined by clinical, radiographic, and PSA criteria. Patients must have good performance status and normal end-organ function. Patients with uncontrolled hypertension and those requiring therapeutic anticoagulation are excluded. All patients are treated with orally administered BAY 43–9006 at a dose of 400 mg bid given continuously on 28-day cycles. Clinical assessment occurs every 28 days with radiographic measurements of disease every 2 cycles. Treatment continues until progression.
Results: This study opened in September 2004 and 19 patients (median age 64 years, range 52–74) have been enrolled to date and all have completed at least 1 cycle of therapy. Grade 3 hand–foot syndrome and grade 3 hypertension have each been noted in 1/19 patients. Drug-related rash has been seen in 3/19 patients and has responded to temporary withdrawal of therapy. Other reported grade 1/2 toxicities include fatigue, flatulence, weight loss, anorexia, body aches, bradycardia, and diarrhea. Fifteen patients are off study due to disease progression. Thirteen patients have been treated for at least 4 months; 5 have exhibited stable disease by both PSA and radiographic criteria.
Conclusions: BAY 43–9006 appears to be well-tolerated in patients with AIPC with a reversible skin rash and hypertension as the most prevalent toxicities. Accrual continues, to better assess the activity and the toxicity profile of this agent.

864 POSTER

Phase II study of BAY 43–9006 (sorafenib) in patients with chemo-naïve hormone refractory prostate cancer

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Background: BAY 43–9006 (BAY) is an orally bioavailable multikinase inhibitor of raf, VEGFR-2, PDGFR, c-kit and ret which prevents tumor cell proliferation and angiogenesis in pre-clinical models. Activation of the MAPK and VEGF signaling pathways have been implicated with androgen independent progression of prostate cancer, and therefore provides a rationale for evaluating BAY in patients (pts) with prostate cancer who have progressed after castration therapy.
Methods: Multi-centre, phase II study using a two-stage design. Pts with hormone refractory prostate cancer with or without documented

metastases, no prior chemotherapy and PSA progression were eligible. BAY was given at a dose of 400mg PO BID continuously on a 28 day cycle. The primary endpoint was PSA response defined as a 50% decrease from baseline for ⩾4 weeks. Paraffin blocks from primary tissue diagnosis are being collected to identify potential predictive markers.
Results: 16 pts were enrolled to the first cohort. ECOG performance status was 0 or 1 in 13 and 3 pts respectively. All pts had evidence of metastases including 12 with bone, 7 with lymph nodes, and 1 with liver. Pts received a median of 3 cycles (1–8). Treatment was generally well tolerated with 2 pts experiencing grade 2 and 3 hypertension, 5 pts hand–foot syndrome (grade 3 in 1 pt), and 7 had fatigue (grade 3 in 1 pt). Grade 3 hematologic toxicity included neutropenia (2 pts), anemia (1 pt) and lymphopenia (1 pt). To date, 1 pt has had a confirmed PSA response (PSA baseline = 10000, nadir = 1643 μg/L) and 4 pts have had post-treatment PSA declines of 37%, 30%, 21% and 5%. 13 pts have discontinued therapy because of progressive PSA/disease. Interestingly, in 4 pts who discontinued BAY and who had not received any other immediate therapy, all 4 had post-discontinuation PSA declines of 15 to 52%. In 7 patients who did receive immediate therapy (3 corticosteroids, 2 palliative radiation, 1 bicalutamide, 1 docetaxel), 6 have had post-discontinuation PSA declines of 19 to 67%.
Conclusions: Post-discontinuation declines in PSA have been observed which may indicate a potential detrimental effect, a positive delayed effect, or an effect on PSA production/secretion by BAY 43–9006. There was evidence of post-treatment PSA declines and further study of BAY 43–9006 in this population is warranted. The criteria for continuing to the second stage of the study have been met and the second cohort of pts is enrolling. Updated results will be presented.

865 POSTER

Zoledronic acid reduces bone loss in men with prostate cancer undergoing androgen blockade with luteinizing hormone-releasing hormone analogues

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Background: Androgen deprivation therapy (ADT) is the primary treatment for patients with hormone-dependent prostate cancer. Goserelin acetate is a synthetic luteinizing hormone-releasing hormone (LHRH) analogue that, when administered in a 10.8-mg depot formulation every 3 months, reduces serum testosterone to levels similar to those found after orchiectomy. However, prolonged ADT with LHRH analogues results in an increased risk for bone loss and is associated with an increased risk of fractures. Zoledronic acid is indicated for the treatment of bone metastases from any solid tumor and has been shown to increase bone mineral density (BMD) in men undergoing initial ADT with a gonadotropin-releasing hormone agonist with or without an antiandrogen. We conducted an open-label, controlled, multicenter study to determine whether treatment with zoledronic acid can prevent bone loss in prostate cancer patients undergoing androgen blockade with goserelin acetate.
Material and methods: Hormone-naive patients with locally advanced prostate cancer (no bone metastases) were randomized in a 1:1 ratio into either a control group receiving goserelin acetate alone every 3 months, or a treatment group receiving 4 mg zoledronic acid+goserelin acetate every 3 months for 1 year. The primary endpoint was the percent change from baseline in lumbar-spine BMD. Secondary endpoints included percent change from baseline in femoral-neck and hip BMD, change in height, and development of bone metastases.
Results: Two hundred men were randomized over a 12-month period ending July 2004. Six-month interim results are available for 51 patients. At 6 months, mean BMD at all sites (lumbar spine, femoral neck, and hip) decreased from baseline in patients treated with goserelin alone. In contrast, mean BMD at 6 months remained stable or increased slightly from baseline in patients treated with goserelin plus zoledronic acid. Overall, patients treated with zoledronic acid+goserelin experienced increases in BMD of up to 1.9% compared with decreases of up to 6.6% in patients treated with goserelin alone. The combination of zoledronic acid+goserelin was safe and well tolerated; the most commonly reported adverse events were hot flashes, nausea, vomiting, and pyrexia. These adverse events were mainly mild to moderate in severity and managed with supportive care.
Conclusions: Zoledronic acid is safe and effective for the treatment and prevention of cancer treatment-induced bone loss in men undergoing ADT with an LHRH analogue.
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866 POSTER

A phase II study of intravesical gemcitabine as adjuvant therapy in patients (pts) with superficial bladder carcinoma: final results

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Background: Systemic intravenous gemcitabine is typically used in advanced bladder carcinoma. A phase I study of intravesical gemcitabine has shown a good safety profile in patients refractory to BCG therapy (Dalbagni G et al JCO 2002; 20:3193–98). In this study, we evaluated the toxicity and the efficacy of intravesical gemcitabine in patients with superficial bladder carcinoma.
Methods: Eligible patients were aged ⩾18 years and had a histological diagnosis of transitional cell carcinoma (TCC) of the bladder (carcinoma in situ or pT1) confirmed by transuretheral resection (TUR). No prior chemotherapy was allowed, and patients had a performance status (PS) <2, adequate organ function and bone marrow reserve, and provided informed consent. Three weeks after a total TUR, patients received intravesical instillation of gemcitabine 2000 mg weekly for 6 weeks, then monthly for 6 months. Evaluation was performed 3–4 weeks after the last instillation (CT scan and/or US pelvis, urinary cytology and cystoscopy with biopsy).
Results: From February 2003 to June 2004, 60 patients (57M/3F) with a median age of 59.5 years (range, 24–84) were enrolled in the study. Nine patients had carcinoma in situ, and 51 had pT1 lesions. All patients were evaluable for toxicity and efficacy. Five patients (8.3%) had a superficial relapse of TCC (1 at 6 months, 2 at 9 months, and 2 at 12 months), and the remaining 55 patients (91.7%) remained disease free after a follow-up period of 26 months. A total of 720 instillations were administered, and grade 1 nonhematologic toxicity included irritative bladder symptoms (4.7%), asthenia (2.9%), hot flashes (2%), and nausea and vomiting (1.8%). Grade 1 hematologic toxicities included anemia (6.8%), leukopenia (4.5%), and thrombocytopenia (0.4%).
Conclusion: Intravesical gemcitabine is an active and well-tolerated adjuvant treatment in patients with superficial TCC of the bladder.

867 POSTER

Alpha-Blocker Alfuzosin (Xatral LA) during radiotherapy for prostate cancer improves radiotherapy induced urinary toxicity

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Purpose/Objective: The main acute toxicity of radical radiotherapy (RT) for prostate cancer is the development of lower urinary tract symptoms (LUTS), which adversely affect patients' quality of life (QoL). This study hypothesis was that α1-uroselective blockers, like alfuzosin, would improve both the symptoms of radiation induced urethritis and also relieve any bladder outlet obstruction due to benign prostatic hyperplasia, and that this improvement in LUTS would result in a benefit in QoL.
Materials/Methods: 50 patients (median age: 65, range: 48–77) were prospectively recruited between October 2001 and September 2004. Neoadjuvant hormonal manipulation was used for 3 months prior and continued whilst on RT, in all but 3 patients. 3D-conformal RT was planned to 74 Gy in 37 fractions in two phases in 45 patients, 5 patients received 64 Gy in one phase. Patients developing bothersome LUTS during RT were started on Alfuzosin 10 mg LA. Prior to starting Alfuzosin, urinary infection was excluded with examination of a urine specimen. Urinary symptoms and QoL were assessed prior, during and after RT using the IPSS, RTOG and ECOG FACT-P QoL questionnaires.
Results: 30 patients developed LUTS and received Alfuzosin; from which 29 are fully evaluable. 19 patients did not develop significant LUTS to merit treatment, whilst one patient refused to take alfuzosin. Paired pre- and post- alfuzosin data is available for 29 patients. There was a significant decrease in the IPSS score following treatment with Alfuzosin ($p = 0.0001$, Wilcoxon signed-rank test), with median IPSS prior to alfuzosin of 18 and median IPSS a week post Alfuzosin of 11. Analysis of the FACT-P global QoL showed no difference, with a trend however for an improvement on the physical domain. From the single question on QoL of the IPSS questionnaire there was a statistically significant difference in QoL between pre and post Alfuzosin ($p = 0.0003$); 17 patients scored an improvement in QoL, whilst one patient scored a deterioration. Similarly there was an improvement in the RTOG grade of toxicity in 22 patients (13 from