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