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

grade II to I, 6 from grade II to 0, 2 from grade I to 0 and 1 from III to II), whilst in one patient there was deterioration. Response was graded as significant (complete or near complete resolution of symptoms) in 16 patients, moderate (partial but noticeable improvement) in 9 and no response (minimal or no improvement) for 4. For those patients that received Alfuzosin during RT for more than 2 weeks, this response was maintained in 16 patients, but was not maintained in 4 patients. Multivariate analysis showed an association of response with prostate volume ($p = 0.041$).
Conclusion: This study confirms that alfuzosin significantly reduces LUTS arising during RT for prostate cancer, and may also improve QoL. This data supports further investigation with a randomized alfuzosin versus placebo study in patients undergoing radical RT for prostate cancer.

868 POSTER

Chemotherapy for teratoma with malignant transformation

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Background: Germ cell tumors (GCT) with a non GCT malignant component is a rare phenomenon called teratoma with malignant transformation (TMT). In the literature, the largest series of patients (pts) with TMT treated with chemotherapy comprises for 12 pts (J Clin Oncol 2003, vol 21, No 23). We report our experience of chemotherapy in 14 patients with TMT.
Patients and methods: Sarcoma was the most frequent histologic type of TMT, identified in 9 pts, with rhabdomyosarcoma ranking first among the subtypes (4/9). Other histological types included adenocarcinoma (4) and bronchoalveolar carcinoma (1). Chemotherapy was administered to 14 pts with TMT, including 10 with measurable disease. Each patient received chemotherapy regimens based on the specific malignant cell observed in the transformed histology.
Results: 7/10 pts with measurable disease achieved a partial response, with the duration of response ranging between 4 and 17 months. Two patients did not respond to treatment and one patient had stable disease. All pts with sarcoma-containing TMT received a cisplatin-doxorubicin based chemotherapy. 9 pts had a resection of residual masses. With a median follow-up of 72 months, 4/14 pts (%) are alive, including 3 who are disease-free.
Conclusion: This is by far the largest reported European experience of chemotherapy in TMT. Although TMT has a poor prognosis compared to GCT, its management may be improved by adapted chemotherapy associated with surgical resection of residual masses.

869 POSTER

Prognostic significance of early predicted time to normalization (TTN) of tumor markers in advanced nonseminomatous germ cell tumors (NSGCT): validation study

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Purpose: K. Fizazi et al. have shown the decline rate of serum AFP and hCG during the first 3 weeks of chemotherapy (CT) predict the outcome in NSGCT pts with poor-prognosis (JCO, Vol.22 (19), 2004). In our validation study we retrospectively studied the prognostic relevance of early predicted TTN in advanced NSGCT.
Patients and methods: During 1984–2002, in the study were included 312 NSGCT chemotherapy (CT)-naïve pts with known tumor markers levels at the beginning of first and second cycles of CT. They were treated with modern cisplatin-etoposide-based CT in our department. Decline rates were calculated using a logarithmic formula and expressed as TTN. Pts with both TTN of AFP <9 wks and hCG <6 wks were defined as favorable group.
Results: Median f.-up time was 36 (range, 12–156) months. Progression-free survival (PFS) and overall survival (OS) were similar in good and intermediate IGCCCG groups irrespective of predicted TTN. In poor prognostic group there was a trend of worsening in 3-years OS in pts who had unfavorable TTN (50%) than favorable TTN (71%, $p = 0.11$). Separate analysis of prognostic relevance of TTN AFP and hCG shown that only unfavorable TTN of AFP predicted lower OS in poor prognostic group in comparison with favorable TTN – 42% and 65% ($p = 0.016$), respectively. According to IGCCCG prognosis OS was entirely identical in pts with favorable or unfavorable TTN of hCG.
Conclusions: The analysis showed that decline rates of AFP but not hCG during the first 3 weeks of CT predict outcome in NSGCT pts with poor-prognosis according to the IGCCCG.

870 POSTER

A pilot study: potential role of nutrient vitamin D in prostate cancer patients with rising PSA after definitive therapy

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Objective: To assess the effect of nutrient vitamin D (cholecalciferol) on the rate of PSA rise and PSA levels in prostate cancer patients with rising PSA after definitive therapy. Optimal management for patients with PSA relapse alone (with no evidence of distant metastasis or local progression) after surgery and/or radiotherapy remains uncertain. Although androgen ablation (AA) has been traditionally the standard treatment for these patients, there are several concerns related to implementing AA in earlier stage of PSA relapse. These include: 1. a finite duration of effectiveness and potentially significant side effects of AA. 2. no randomized study suggesting the benefit of immediate AA for PSA relapse alone, compared with delayed application at the time of clinical evidence of tumor progression. Thus many clinicians choose to observe asymptomatic patients with PSA relapse alone. On the other hand, it is distressful to a patient to be idle in the presence of rising PSA. Therefore it is desirable to have an agent with low toxicity that can inhibit or decrease the rate of tumor progression before consideration of AA. Vitamin D may be such an agent.
Methods: A prospective, single arm, study. Fifteen asymptomatic patients (median age: 68) with PSA relapse alone after surgery and/or radiotherapy were treated with simple, nutritional vitamin D 2000 IU per day orally. All had an evidence of PSA relapse with at least 3 successive PSA rises over a minimum of 9 months after definitive therapy. Patients were followed every 2–3 months for PSA levels and toxicity. The rates of PSA rise and absolute PSA levels were compared between before and after the initiation of vitamin D.
Results: Median follow-up after the start of vitamin D was 8 months (range:4–21). 8/15 had a decrease in PSA (sustained from 5 to 17 months) after the start of vitamin D. In one additional patient, PSA levels fluctuated around the baseline for 21 months. After the start of vitamin D, 14/15 had a decrease in the rate of PSA rise, which was statistically significant ($p = 0.005$). PSA doubling time increased from a median of 14.3 months before vitamin D to 25 months after vitamin D. None had side effects from vitamin D.
Conclusion: Simple, nutrient vitamin D appears an effective agent that can moderate the rate of PSA rise, which may suggest the retardation of tumor progression. This was achieved with very low cost ($2.00/month) and no adverse effects. A confirmatory study is needed.

871 POSTER

Urinary ICAM-1 levels can predict response in superficial bladder cancer treated with intravesical immunotherapy

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Aim: The present study investigated the value of urinary ICAM-1 as a prognosticator of response in patients with superficial bladder cancer treated with different immunotherapeutic modalities.
Material and methods: 34 patients with histologically proven superficial recurrent bladder cancer (except carcinoma in situ) were included in the study. The patients received intravesical instillations of bacillus Calmette-Guérin (BCG), interferon-α-2b and interferon-γ-1b. Three fresh-voided urine specimens were collected from every patient at each instillation; one before the instillation, one 12 hours after the instillation and one 24 hours after the instillation. ICAM-1 measurements in the urine were performed using a commercially available enzyme-linked immunosorbent assay (ELISA) kit. Response to treatment was evaluated with cystoscopy and routine urine cytology every 3 months for a period of 12 months. Patients without evidence of recurrence were considered as responders, whereas those with recurrent disease were considered as non-responders.
Results: Mean urinary soluble ICAM-1 levels at each instillation were calculated from the three pertinent measurements. Concentrations in the