efficacy and toxicity of different VRL schedule administered as a fixed-weekly dose of 60 mg/m^2. The purpose of this study was to evaluate the toxicity profile and efficacy of this schedule in terms of PSA response, objective response and clinical benefit (CB) response.
Methods: Pts characteristics were: PS 0−2, adequate bone marrow, liver and renal functions. Oral VRL was adminestered at weekly dose of 60 mg/m^2 until disease progression/intolerable toxicity. PSA response was defined as a >50% fall in PSA from baseline, confirmed by a second PSA value 4 or > weeks later. Pts with measurable soft tissue disease met traditional guidelines for tumour responses. Progression was defined by objective disease progression or PSA increase of >50% above nadir or >25% above baseline. Pts were monitored clinically and with serial PSA measurements every 1 week.
Results: Thirty seven pts with progressive HR metastatic prostate cancer were evaluated. Mean (range) age was 67 years (50−88), median PSA level was 90 ng/ml(1− 4314), and median Gleason score was 7 (6−9). 23 (62%) pts had previous taxane chemotherapy and 14 pts (38%) were chemo-naive. Pts received a mean of 5.5 cycles (1cycle = 3wks) (range:1−24). Median follow-up was 12 months. Thirty three of 37 Pts (97%) achieved a decline in serum PSA. CB response was achieved in 15 out of 37 pts(40%). The PSA response was observed in 13 pts (35%). Objective response was not observed and only 6 pts showed SD (16%). The relative dose-intensity was 94%. There were no reported grade 3−4 toxicities. Only 1 treatment discontinuation was observed (esopahgitis g2). Toxicities consisted primarily of g2 anemia (25%) and mild nausea (32%).
Conclusions: Oral Vinorelbine administered as a fixed-weekly schedule of 60 mg/m^2 is a safe regimen in pts with advanced HRPC. This regimen of oral vinorelbine is an effective and well-tolerated treatment in this setting, despite a major dose-intensity administered. Further studies will be evaluated in chemo-naive and/or elderly population.

7039 POSTER

MRI based dose escalation in patients treated with salvage radiotherapy after radical prostatectomy for prostate cancer

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Purpose: We evaluated the treatment results and morbidities in patients treated with selective dose according to existence of recurrent lesions in MRI for salvage radiotherapy (RT) after radical prostatectomy (RP) of prostate cancer.
Materials and Methods: Between 2000 and 2006, 50 patients underwent salvage RT alone for PSA failure after RP. Before salvage RT, all patients were examined with MRI prospectively. Radiotherapy was done with 3D-CRT confined to the prostate bed. Irradiated dose was 66 Gy in patients without suspected gross tumor (low-dose group) or 70 Gy in patients with suspected gross tumor in MRI (high-dose group) with daily 2.0 Gy. Biochemical failure after salvage RT defined as a serum PSA value > 0.2 ng/ml above the post-RT PSA nadir. The toxicity was evaluated by Common Terminology Criteria for Adverse Events (CTCAE) version 3.0.
Results: Median follow-up was 34 months (range: 21−99 months). Seventeen patients (34 %) experienced PSA failure and 3 (6 %) patients developed distant metastases during follow-up. The 3-year and 5-year PSA failure free survival rate was 67.1 % and 55.9% respectively. According to irradiated dose, 3-year PSA failure free survival rate was high in high-dose group, compared with low-dose group, but not significant (68.9 %:64.9 %, $p = 0.70$). The only affecting factor for PSA failure after salvage RT was pre-RT PSA level. PSA failure rate was significantly high in pre-RT PSA >1 ng/ml compared with pre-RT PSA $\leqslant$1 ng/ml (58 %:26 %, $p = 0.041$). In multivariate analysis, pre-RT PSA level was the only significant prognostic factor affecting for PSA failure rate ($p = 0.025$). During follow-up, four patients (8%) developed grade 2 toxicities that included 3 patients of incontinence and 1 patient of hematuria. There was no grade 3 or greater treatment-related toxicities.
Conclusions: In this study, high-dose group (suspected gross tumour) showed similar PSA failure free survival rate, compared with low-dose group (no suspected gross tumour). MRI evaluation before salvage RT might be useful to evaluate the disease status and to determine irradiated dose. However, the optimal dose according to disease status after PSA failure is still controversial. Further studies are needed to determine optimal irradiated dose for salvage RT in patients treated with RP according to the disease status and the benefit of combined treatment with hormonal therapy in patients with pre-RT PSA level above >1 ng/ml.

7040 POSTER

Honokiol, a natural plant product from magnolia tree, inhibits the bone metastatic growth of human prostate cancer cells

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Background: Honokiol, a soluble nontoxic natural product derived from Magnolia spp., was reported to induce apoptosis in caner cells. In this study, we investigated the effect of honokiol and the combined with docetaxel on prostate cancer (PCa) growth and its bone metastasis in experimental models.
Materials and Methods: We investigated in vitro proapoptotic effects of honokiol on human androgen-dependent and -independent PCa, bone marrow, bone marrow-derived endothelial, and prostate stroma cells. Honokiol-induced activation of caspases was evaluated by FACS analysis and Western blot. Mice bone was inoculated in vivo with androgen-independent PCa, C4−2 cells and the effects of honokiol and/or docetaxel on PCa growth in bone were evaluated. Daily honokiol (100 mg/kg) and/or weekly docetaxel (5 mg/kg) were injected intraperitoneally for 6 weeks. PCa growth in mouse bone was evaluated by radiography, serum prostate-specific antigen (PSA), and tissue immunohistochemistry regarding the markers of cell proliferation, apoptosis, and angiogenesis.
Results: Honokiol inhibited cell growth through the induction of apoptosis in all cell lines tested. In PCa cells honokiol-induced apoptosis was via the activation of caspases 3, 8, and 9, and the cleavage of poly-adenosine diphosphate ribose polymerase in a dose- and time-dependent manner. Honokiol was shown to inhibit the growth and depress serum PSA in mice harboring C4−2 xenografts in the bone and the combination with docetaxel showed additive effects that inhibited further growth without evidence of systemic toxicity. Immunohistochemical staining confirmed honokiol exhibited growth-inhibitory, apoptotic, and antiangiogenic effects on PCa xenografts.
Conclusions: The combined therapy of honokiol and low-dose docetaxel may improve patients' outcome in androgen-independent prostate cancer with bone metastasis.

7041 POSTER

Active potential of sonic Hedgehog signaling between human prostate cancer cells and normal/benign but not cancer-associated human prostate stromal cells

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Backgrounds: Sonic hedgehog (Shh) signaling is known to affect normal prostate development and possibly mediate prostate cancer-stromal interaction. We investigated Shh signaling between human prostate cancer cells and prostate stromal cells isolated from normal/benign and malignant tissues and determined the downstream *stromal targets* of this interaction.
Materials and Methods: Shh and its downstream target transcription factor, Gli1 mRNAs was assessed by RT-PCR in prostate stromal cells established from normal/benign (NPF), cancer-associated areas (CPF), or human bone marrow stromal (HS27A) cells in cell culture containing recombinant Shh. Co-culture and conditioned medium (CM) studies were also conducted to determine the effects of Shh on C4−2 cell growth using C4−2-Luc cells stably transfected with Luciferase gene, in the presence or absence of cyclopamine, Shh-Gli1 signaling inhibitor. The Results were confirmed by *in vivo* studies in chimeric subcutaneous prostate tumors comprised of C4−2-Luc and NPF.
Results: Recombinant Shh induced Gli1 expression in cultured NPF but not CPF, HS27A or C4−2 as evaluated by RT-PCR. Shh stimulated C4−2-Luc growth when co-cultured with NPF but not CPF nor HS27A, and this effect was completely abrogated by cyclopamine. We have also shown that osteonectin (ON) expression is induced by Shh in stromal cell. Although C4−2 cells expressed Shh and its expression level was not affected by exogenous added Shh, the CM of C4−2 induced growth of NPF, not CPF, and this induction was completely blocked by cyclopamine. A chimeric tumor of C4−2 and NPF demonstrated to respond to cyclopamine