PSA from baseline. In Cohort 3, 7 of 9 pts are still on treatment after 2 cycles, with 1 patient having a 99% PSA reduction at Cycle 4. Of the 13 pts enrolled with measurable disease, 2 pts have achieved an unconfirmed partial response and 6 pts have unconfirmed stable disease using RECIST criteria.
Conclusions: The maximal dose of panobinostat allowed by the protocol in combination with docetaxel and prednisone is 20 mg/m^2. The combination is well tolerated and has shown promising activity both for PSA reduction and tumor shrinkage. The combination warrants further exploration in a randomized Phase II setting.

7025 POSTER

Prognostic value of hypermethylation for retinoic acid receptor beta (RARB) and p-16 genes in patients with prostate cancer

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Background: Correlations between specific gene hypermethylation and clinicopathologic features suggestive of aggressive disease characteristics indicate that these genes may have prognostic potential. Such molecular markers may help to identify men who will undergo recurrence, so that they can be targeted for more aggressive therapy. we investigated hypermethylation of promoter genes, retinoic acid receptor β (RARB) and p-16, prostate cancer patients with different prognostic features who referred to three hospital in Iran between Jan 2007 and April 2008.
Methods: 63 prostate biopsy specimens from three different groups of patients, 21 benign prostate hyperthrophy (BPH) as control group, 21 prostate cancer who had good prognostic features, and 21 patients with poor prognostic feature were evaluated. The prostate biopsy specimen examined for hypermethylation of promoter genes RARB and p-16 with Methylation Specific PCR (MSPCR) and odds ratio for any association with patients' prognosis were tested by Chi-square and Fisher exact test.
Results: There was no RARB methylation in BPH specimens. In patients with good prognostic features 7 (33.3%) were positive for RARB methylation which was significantly more common than control group ($p < 0.000001$).RARB methylation was found in 15 (71.4%) of patients specimens with poor prognostic features, that were more common than control group (0.000001). The RARB methylation in patients with poor prognostic factors were significantly more common than in patients with good prognostic features ($p < 0.02$). There was no p-16 positive subject in BPH group. In patients with good prognostic features 19% had methylation of p-16 and of those with poor prognostic features 47.6% were positive for RARB methylation. The P16 methylation in patients with poor prognostic factors were significantly more common than in patients with good prognostic features($p < 0.00001$).
Conclusion: Methylation of RARB and p-16 are good indicator for early detection and predicting prognosis of prostate cancer in Iranian patients.

7026 POSTER

Deriving prostate alpha-beta ratio using carefully matched groups, long follow-up and the Phoenix definition of biochemical failure

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Background: Prior studies derived a low value of a/β for prostate cancer (e.g. 1−2 Gy) using outcome data from external beam radiotherapy (EBRT) and permanent prostate brachytherapy (PPB). However, these values are associated with wide confidence intervals and inaccuracies such as poorly-matched groups, differing definitions of biochemical failure and insufficient follow-up.
Materials and Methods: Patients with Canadian Consensus Risk Group low- or low-tier intermediate risk prostate cancer, treated with either EBRT or PPB, were matched for PSA, Gleason score, T-stage, percentage of positive cores, androgen deprivation therapy duration and era, yielding 118 pairs. The Phoenix definition of biochemical failure was used. The best value for a/β was found using maximum likelihood analysis, and 95% confidence intervals using the profile likelihood method. The linear quadratic formalism was applied with radiobiological parameters set at RBE = 1, Tpot = 45 days, and repair half-time = 1 hour. Sensitivity analysis was performed using extreme values of these parameters.
Results: PPB and EBRT groups were well-matched with respect to all known risk factors. Median follow-up or time to failure was 60 months. Kaplan-Meier estimates of freedom from biochemical failure (bNED) showed superiority of PPB compared to EBRT (log-rank test $p = 0.001$): Estimates of probability of bNED were 82% and 95% at 72 months for EBRT and PPB; and 63% and 95% at 90 months. The value of a/β that best fitted the outcome data was >30 Gy, with a lower 95% confidence limit of 3.2 Gy. This was confirmed on bootstrap analysis. Varying the parameters to extreme values yielded a best-fit a/β of at least 3.0 Gy.
Conclusions: Our result of >30 Gy as the best estimate of a/β for low and low-intermediate risk prostate cancer directly contrasts with prior best estimates of 1−2 Gy. Obtained values of a/β result from superior outcomes for PPB observed for long follow-up time. If the true value of a/β is not less than the rectal a/β then radiation hypofractionation may not improve the therapeutic ratio.

7027 POSTER

Interim results of a phase II trial of oxaliplatin and pemetrexed as 2nd/3rd line therapy in castration resistant prostate cancer (CRPC)

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Background: There is no standard of care for men with metastatic CRPC after disease progression on docetaxel. Pemetrexed and oxaliplatin have each shown modest single-agent response rates in CRPC and have non-overlapping toxicities; this trial evaluates their efficacy in combination.
Methods: Men with CRPC whose disease progressed on docetaxel were eligible. A two-stage design ($\alpha = 0.1$, $\beta = 0.1$) was used to determine the response rate as primary endpoint (RECIST, or PSA if no measurable disease present); 47 patients are planned. After giving written informed consent, 31 men enrolled from July 2006 - November 2008. Treatment was pemetrexed 500 mg/m^2 IV and oxaliplatin 120 mg/m^2 IV every 3 weeks, with folate and B12 supplementation.

Response	Number (%)
Overall (N = 31)	
PR (>50% decrease PSA or RECIST)	10 (32%)
SD	12 (39%)
PD	6 (19%)
Inevaluable – off treatment	4 (13%)
RECIST (N = 26)	
PR	4 (15%)
SD/unconfirmed PR	18 (58%)
PD	4 (13%)
Inevaluable	5 (16%)

Toxicity	Grade 1/2	Grade 3/4
Allergic	7	1
Auditory	12	0
Bone Marrow	22	8
Constitutional	22	6
Dermatologic	5	0
Gastrointestinal	24	0
Hemorrhage	5	0
Hepatic (including alk phos)	23	4*
Metabolic/Laboratory	12	0
Neurologic (dizziness, confusion, ataxia)	18	5
Pain	7	3
Pulmonary	2	1
Renal	4	0

*2 grade 3 AST/ALT

Results: Median age was 66 (41−81), 72% were Caucasian and 97% had ECOG performance status 0−1. Median baseline PSA was 286 ng/mL (range 4.8−2290). All had metastatic disease with 1 (55%) or 2 (45%) prior chemotherapy regimens; 94% had bone involvement. Subjects received a median of 6 treatment cycles (range 1−21); 3 continue on study. Responses are summarized in the table; 8 of the 31 patients (26%) have achieved a PSA response, and 4 objective PRs by RECIST, out of 26 evaluable patients. Eighteen (58%) had stable disease. After 15 deaths, median survival is 11.8 months (95% CI 7.5−23.5+). Toxicities are presented in the table; the only grade 4 event was thrombocytopenia. Common grade 3 events included fatigue (6 subjects), hematologic (7), and neurologic (5). Two patients died while on study, one due to disease progression and the other one due to cardiopulmonary arrest.