13 months, the addition of BEV to IFN-α 2a significantly improved duration of PFS in all evaluable patients (10.2 vs 5.4 months, HR = 0.63, p < 0.0001). Analysis of PFS in the prespecified patient subgroups showed that the hazard ratio was consistently <1.
Conclusions: These results demonstrate that BEV plus IFN-α 2a provides a consistent clinical benefit irrespective of baseline prognosis factors and patient characteristics.

4009 POSTER

Urine is the preferred remote body fluid for early identification of prostate cancer using real-time PCR detection of DNA methylation markers

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Background: A prostate cancer (PCa) screening biomarker with improved specificity relative to PSA or with the diagnostic ability to discriminate PCa from BPH in patients with elevated PSA would offer a valuable tool for the public health management of PCa. Aberrant DNA methylation occurs early in tumorigenesis, is stable, and can be assayed in tissues and body fluids, making targets of aberrant DNA methylation attractive biomarker candidates. We previously identified candidate DNA methylation markers to discriminate PCa from benign epithelium. We have now validated those markers in a clinical trial and determined the optimal remote body fluid for PCa screening and diagnostics.
Materials & Methods: A clinical study was initiated to determine the optimal remote analyte for a methylation biomarker and to validate the performance of real-time quantitative HeavyMethyl® PCR assays associated with the genes GSTP1, RASSF2, HIST1H4Kand TFAP2E in body fluids. Matched plasma and urine were collected from 100 PCa patients, 51 biopsy negative patients (diagnosed with BPH subsequent to biopsy referral for elevated PSA) and 50 young healthy control males with no known family history of PCa. ROC curves were generated for each marker and cut-off values for methylation were optimized.
Results: In all negative class comparisons and for all markers, urine was the more sensitive analyte. RASSF2 was the best performing screening marker candidate with 74% sensitivity at 96% specificity in urine (37% sens, 100% spec in plasma). HIST1H4K was the best performing diagnostic marker candidate with 28% sensitivity at 95% specificity in urine (16% sens, 96% spec in plasma). None of the markers correlated with PSA values, indicating that they contribute additional information not provided by the PSA value alone. All markers correlated with Gleason score in both urine and plasma DNA. A quantitative screening panel of markers RASSF2 and HIST1H4K yielded 94% sensitivity at 88% specificity. A quantitative diagnostic panel of markers GSTP1 and PSA yielded 83% sensitivity at 45% specificity.
Conclusions: In a series of matched urine and plasma samples we have shown that urine is a superior remote analyte for PCa detection and diagnosis as compared to plasma. We have also shown that a screening panel of only two markers can achieve 94% sens with a spec of 88%. While we have clearly identified markers that discriminate PCa patients from healthy controls, the current markers do not sufficiently discriminate PCa patients from those with BPH as a diagnostic follow-on test to PSA. Identification of markers that improve discrimination of PCa from BPH with elevated PSA is currently underway.

4010 POSTER

Satraplatin increases progression-free survival (PFS) and delays pain progression in hormone refractory prostate cancer (HRPC): Results of SPARC, an international phase III trial with 950 patients

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Background: Satraplatin (S) is a novel oral platinum agent with demonstrated activity in many tumors, including HRPC. The SPARC study, a large, randomized, phase III trial, was conducted to compare the effects of S + prednisone (P) and placebo (PL) + P in patients (pts) with HRPC who had failed 1 prior chemotherapy regimen.
Methods: Eligible pts were had stage D2 metastatic HRPC and ECOG performance status 0−2. Pts were randomized to S (80 mg/m^2 qd × 5 d q5w) +P (5 mg bid qd) or to PL+P. The primary endpoint was PFS. Secondary endpoints included time to pain progression (TPP), as indicated by increased present pain index (PPI) score or increased opioid use, and PSA response (⩾50% reduction from baseline). Exploratory analyses measured PFS and TPP for subsets of pts based on prognostic variables: age (<65 or ⩾65 years), baseline PPI score (0 or ⩾1), baseline ECOG score (0−1 or 2), prior docetaxel use, type of tumor progression, and bisphosphonate use.
Results: 950 pts were randomized to S (n = 635) or PL (n = 315). Most pts were Caucasian (89%), age ⩾65 years (71%, median 70 yrs), ECOG score 0−1 (90%), and PPI score 0−1 (65%). In the ITT analyses, pts in the S arm had 33% reduced risk of PFS or death vs the PL arm (median 11.1 vs 9.7 weeks, respectively; HR = 0.67, 95% CI: 0.57−0.77; p < 0.001) and significantly longer median TPP (66.1 vs 22.3 weeks, respectively, HR = 0.64, 95% CI: 0.51, 0.79; p < 0.001). PSA response was also significantly higher in the S arm (25.4% vs 12.4%, p < 0.001). Robust findings across patient subgroups showed significant and comparable treatment effects of S on PFS and TPP irrespective of prior docetaxel use, age, or bisphosphonate use; as well as in pts with baseline PPI scores ⩾1, ECOG scores 0−1, and pts with tumor progression with or without PSA increase. S was well tolerated; the most common adverse events were mild to moderate myelosuppression and GI disturbances. When analyzed by age, neutropenia was more frequent in pts ⩾75 yrs, but no pt in this group had febrile neutropenia and the overall incidence of Grade 3−4 infections remained low.
Conclusions: Second line chemotherapy for pts with HRPC is an unmet medical need. Benefits of satraplatin use on PFS, TPP, and PSA in the ITT population are clear. These results are highly robust. Comparable treatment effects are revealed in different subsets of pts defined by prognostic variables. Satraplatin is well tolerated and will be a welcome addition to the therapeutic armamentarium.

4011 POSTER

Results of a phase 3, randomized study of patients with advanced renal cell carcinoma (RCC) and poor prognostic features treated with temsirolimus, interferon-α or the combination of temsirolimus + interferon-α

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Background: Temsirolimus is a specific inhibitor of mTOR, a signaling protein that regulates cell growth and angiogenesis. A phase 3, randomized study was designed to determine the effects of first-line treatment with temsirolimus, interferon-α (IFN), or the combination temsirolimus + IFN on patients (pts) with advanced RCC and poor prognostic features. In a second interim analysis, the O'Brien-Fleming Boundary for early success was crossed for the primary endpoint of overall survival (OS; Hudes et al. J Clin Oncol 24: LBA4, 2006). Pts receiving temsirolimus had significantly longer OS compared with IFN (hazard ratio [HR] 0.73; 95% confidence interval [CI] 0.57−0.92; p = 0.007). Pts receiving temsirolimus + IFN did not have significantly longer OS compared with IFN (HR 0.95; 95% CI 0.76, 1.20; p = 0.691). We report the final supportive analysis of this study.
Methods: Pts with previously untreated RCC and poor prognostic features (⩾3 of 6 prognostic factors [Hudes et al. J Clin Oncol 24:LBA4, 2006]) were randomly assigned to 1 of 3 treatment arms: temsirolimus 25 mg IV once weekly (n = 209); IFN 3 million units (MU) escalating to 18 MU subcutaneously (SC) 3 times weekly (n = 207); or temsirolimus 15 mg IV once weekly + IFN 6 MU SC 3 times weekly (n = 210).
Results: This final supportive analysis of 626 pts enrolled was completed when 514 deaths had occurred and confirmed the results of the second interim analysis. Pts receiving temsirolimus continued to have longer OS compared with IFN (HR 0.78; 95% CI 0.63, 0.97; p = 0.0252). OS of pts receiving temsirolimus + IFN was not significantly longer than that for pts receiving IFN (HR 0.93; 95% CI 0.75, 1.15; p = 0.4902). Median OS for temsirolimus, IFN, and combination groups was 10.9, 7.3, and 8.4 months, respectively. Progression-free survival (PFS; investigator assessed) was significantly longer for pts receiving temsirolimus vs. IFN (HR 0.74; 95% CI 0.60, 0.90; p = 0.003). Median PFS was 3.8 and 1.9 months, respectively.