

MP02-19: Biomarkers of biochemical (BCR) and clinical recurrence (cR) in prostate cancer (PCa) following radical prostatectomy (RP) – performance of a 17-gene genomic prostate score (GPS) and tests for PTEN loss.

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Introduction and Objectives

PTEN loss by fluorescence in situ hybridization (FISH) or immunohistochemistry (IHC) has been reported in 20-60% of localized PCa and is viewed as an adverse prognostic factor. The GPS (scale 0-100) is an analytically and clinically validated RT-PCR assay that measures tumor aggressiveness in biopsies of men with early stage PCa. Gene selection for GPS was based on the strength of association between their expression and clinical outcomes and PTEN RNA expression was evaluated but not included in the GPS signature. The prognostic value of GPS and PTEN loss as determined by IHC and FISH in predicting cR and BCR after RP for clinically localized PCa was assessed.

Methods

RPs from 441 AUA low, intermediate and high risk disease patients were used to develop GPS. PTEN status was assessed by FISH and IHC in 287 and 369 of these patients, respectively, using tissue microarrays. PTEN FISH loss was defined as hemizygous or homozygous deletion; PTEN IHC loss was defined as homogeneous loss of staining. GPS was generated using tumor RNA from microdissected RPs. Multivariable Cox models were used to analyze BCR and cR (defined as distant or local recurrence), and regression to the mean correction was used for GPS.

Results

38% of patients had PTEN loss by FISH and 25% by IHC, and evaluable patients were representative of the full cohort. While PTEN status by FISH or IHC was associated with BCR ($p < 0.001$) and cR ($p < 0.05$) in univariate analysis, after adjusting for GPS, neither FISH nor IHC PTEN was a significant predictor of either BCR ($p > 0.05$) or cR ($p > 0.1$). Concordance between the 2 PTEN methodologies was 66% ($p < 0.001$), whereas PTEN status and GPS were only weakly correlated (Spearman $\text{corr} = 0.2$ - FISH, 0.3 - IHC) and a broad range of overlapping GPS was observed in each PTEN category. GPS remained very strongly associated with cR and BCR after adjusting for PTEN [HR/20 units = CR 4.0 (95% CI 2.1, 7.6), BCR 2.1 (95% CI 1.3-3.3) by FISH; HR/20 units = CR 4.0 (2.3, 6.7), BCR 1.6 (95% CI 1.1-2.3) by IHC]. Of PTEN deleted cases (by FISH), 31% with the lowest GPS had <2% 10-year rate of cR. Of PTEN intact cases (by FISH), 29% with the highest GPS had a 14% 10-year rate of cR.

Conclusions

GPS is a significant predictor of BCR and cR following RP after adjustment for PTEN status assessed by FISH or IHC. PTEN is not a significant predictor of BCR or cR after adjustment for GPS. GPS can identify a group of PTEN loss patients with a very favorable prognosis and a group of PTEN intact patients with unfavorable prognosis