Validation of a Metastatic Assay using biopsies to improve risk stratification in patients with prostate cancer treated with radical radiation therapy

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Background

Radiotherapy is an effective treatment for intermediate/high-risk locally-advanced prostate cancer, however, >30% of patients relapse within five years. Clinicopathological parameters currently fail to identify patients prone to systemic relapse and those whom treatment intensification may be beneficial. The purpose of this study was to independently validate the performance of a 70-gene Metastatic Assay in a cohort of diagnostic biopsies from patients treated with radical radiotherapy and androgen deprivation therapy (ADT).

Methods

A bridging cohort of prostate cancer diagnostic biopsy specimens was profiled and used to enable optimization of the Metastatic Assay threshold prior to further independent clinical validation in a cohort of diagnostic biopsies from patients treated with radical radiotherapy and ADT. Multivariable Cox proportional hazard regression analysis was used to assess assay performance in predicting biochemical failure-free survival (BFFS) and metastasis-free survival (MFS).

Results

Gene expression analysis was performed in 248 patients from the independent validation cohort and the Metastatic Assay applied. Ten year MFS was 72% for Metastatic Assay positive patients and 94% for Metastatic Assay negative patients (HR=3.21, [1.35-7.67]; p=0.003). On multivariable analysis the Metastatic Assay remained predictive for development of distant metastases (HR=2.83, [1.13-7.11]; p=0.027). The assay retained independent prognostic performance for MFS when assessed with the Cancer of the Prostate Assessment Score (CAPRA) (HR=3.23 [1.22-8.59]; p=0.019) whilst CAPRA itself was not significant (HR=1.88, [0.52–6.77]; p=0.332). A high concordance (100% [61.5-100]) for the assay result was noted between two separate foci taken from 11 tumors, whilst Gleason score had low concordance.

Conclusions

The Metastatic Assay demonstrated significant prognostic performance in patients treated with radical radiotherapy both alone and independent of standard clinical and pathological variables. The Metastatic Assay could have clinical utility when deciding upon treatment intensification in high-risk patients.

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Disclosures

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