Editorial

New genomic markers for improved decision making in the prostate cancer active surveillance era

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Active surveillance (AS) for men with low risk prostate cancer (PCa) has emerged as one of the accepted management options over the last decade. Even though it has been widely implemented, the process of selecting appropriate patients remains somewhat ambiguous due to lack of unanimously established criteria. Currently, such criteria are mainly based on clinicopathologic variables [such as Gleason score, prostate specific antigen (PSA), clinical stage, PSA density, percent of needle cores that contain cancer], whose definitions vary between different institutions and academic centers. What complicates the issue even further is the current practice of trans-rectal ultrasound guided prostate needle biopsy which may miss higher grade disease in up to 27% of men (1), and furthermore a 36% discrepancy rate of appropriate grading of PCa among different pathologists (2). Taken together, this may adversely affect choice of therapy and ultimately patient outcomes. Although new technological advances related to the multiparametric magnetic resonance imaging (MRI) of prostate are being applied to resolve some of the problems, the learning curve has been noted to be steep and requires dedicated teams of radiologists for successful outcomes. As a result, enormous efforts to find better prognostic tools are under way.

Recently, new tumor-based molecular assays such as Decipher (GenomeDx, San Diego, CA, USA), Oncotype Dx (Genomic Health, Redwood City, CA, USA), Prolaris (Myriad Genetics, Salt Lake City, UT, USA), and ProMark (Metamark, Waltham, MA, USA) have been shown to provide prognostic information independent of clinicopathologic based risk groups, and therefore are becoming incorporated in the decision-making process (3). The article by Lin *et al.* describes yet another promising molecular based test which combines both molecular and clinical information to provide a clinical cell-cycle risk (CCR) score, ultimately improving prostate-cancer specific mortality risk stratification (4). Their results showed that CCR scores below the selected threshold had a predicted mean 10-year PCa mortality of 2.7% and significantly dichotomized low- and high-risk disease. Importantly, their test also identified a substantially higher number of patients as candidates for AS (68%) compared to clinicopathologic features alone (42%). One of the potential biases of current study is the retrospective nature of patient cohort selection, however, the authors tried to include subjects from multiple independent cancer registries and employ disease population-based sample collection to reduce potential bias. Additionally, their validation cohort was not a true AS cohort, but instead it was composed of men who deferred curative therapy. Such biases are not specific to this study only, but plague most of the other recently developed molecular tests and therefore must be carefully interpreted.

Clearly, long-term prospective studies and data collection will shed more light on such tests and the appropriate incorporation into AS protocols. At present time, we also lack studies on large scale cost effectiveness and cost utility of such tests to be able to understand their potential economic

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benefit in addition to their clinical utility. Ultimately, the idea behind these tests is not only to help decrease over-diagnosis and -treatment of men with PCa, but also to reduce medical costs and improve patients' quality of life.

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