Mismatch Repair Deficiency is Common in Ductal Adenocarcinoma of the Prostate

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Background: Precision oncology entails making treatment decisions based on a tumor's molecular characteristics. For prostate cancer, identifying clinically relevant molecular subgroups is challenging, as molecular profiling is not routine outside of academic centers. Since histologic variants of other cancers correlates with specific genomic alterations, we sought to determine if ductal adenocarcinoma of the prostate (dPC) – a rare and aggressive histopathologic variant – was associated with any recurrent actionable mutations.

Methods: Tumors from consecutive patients with dPC were sequenced on a targeted next-generation DNA sequencing panel.

Results: Tumors from 10 patients with known dPC were sequenced. The median age at diagnosis was 59 years (range, 40-73). Four (40%) patients had metastases upon presentation. Archival tissue from formalin-fixed paraffin-embedded prostate tissue samples from nine patients and a biopsy of a metastasis from one patient with castration-resistant prostate cancer were available for analysis. Nine of 10 samples had sufficient material for tumor sequencing. Four (40%) patients' tumors had a mismatch repair (MMR) gene alteration (N=2, *MSH2*; N=1, *MSH6*; and N=1, *MLH1*), of which 3 (75%) had evidence of hypermutation. Sections of the primary carcinomas of three additional patients with known MMR gene alterations/hypermutation were histologically evaluated; two of these tumors had dPC.

Conclusions: MMR mutations associated with hypermutation were common in our cohort of dPC patients. Since hypermutation may predict for response to immune checkpoint blockade, the presence of dPC may be a rapid means to enrich populations for further screening. Given our small sample size, these findings require replication.

Conflict of Interest: None

Funding Acknowledgements: We acknowledge funding support from PNW Prostate SPORE CA097186; DOD awards PC131820, W81XWH-15-1-0562 and W81XWH-15-1-0430; NCI Cancer Center Support Grant 5P30 CA015704-40; the Prostate Cancer Foundation (including Young Investigator Awards to MTS, HHC, and CCP); and an award from the FHCRC Solid Tumor Translational Research Program.