There are few therapy options for advanced refractory prostate cancer. Recent data have shown metastatic prostate cancer patients:
- with DNA repair deficiencies (BRCA, ATM) respond to PARP inhibitors (olaparib)
- have longer overall survival when treated with chemotherapy (docetaxel)
- TOP2A, EGFR (1+)
- Visceral (3+)
- 40-71
- Polkinghorn 71-80
- 51-60
- 1+
- 35.0
- PDL1
- Non-Visceral
- tested specifically in DRD PC.

Methods: Molecular profiles of 437 PC tumor samples were defined. Protein expression (IHC), gene amplification (ISH) and sequencing (NGS) were performed. A panel of 30 DNA repair genes was used to define DNA repair intact (DRI) and DNA repair deficient (DRD) subgroups. Unclassified variants were included for analysis.

Results: Biopsies from 437 PCs (median age 67) were studied. Specimens submitted for profiling included 158 P PCs (36%) and 279 M PCs (64%) (186% (186%); 37% (37%); 24% (24%); 21% (21% other sites)). The most frequently mutated DNA repair genes included TP53 (31%), ERCC3 (19%), FANCJ (16%), MSH6 (13%), POLE (10%), PMS1 (13%), Pten (9%) and BRCA2 (6%). Functional protein loss as measured by IHC was seen in ERCC1 (44%), MGMT (43%), and PPTEN (43%). 518 advanced prostate cancer patients were included in this analysis and tested centrally at a CLIA laboratory (Caris Life Sciences, Phoenix, AZ). Tissues included one or more of the following: gene sequencing MiSeq and NextSeq (Iluminia platforms), copy-number variation (IntelliSeq Exome) and protein expression (immunohistochemistry (IHC)).

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Conclusions: DNA repair defects are common in PC with a difference in gene expression and mutation between P and M tumors.

Differential expression between African American and Caucasian patients and further classification of variants are currently being assessed. Taxane-platinum combination chemotherapy should be tested specifically in DRD PC.

References: