Validation of Nuclear-Localized AR-V7 on Circulating Tumor Cells (CTC) as a Treatment-Selection Biomarker for Managing Metastatic Castration-Resistant Prostate Cancer (mCRPC)

Background
- After 1st line failure of an androgen receptor signaling inhibitor (ARsi: abiraterone, enzalutamide) most patients given a trial of another ARsi
- Overall response rates are lower but a proportion do respond, who can not be predicted based on the response to the first drug administered
- Needed are biomarkers to predict who is better (most likely to benefit) from a taxane or an ARsi, at the individual level in the 2nd line of mCRPC
- In a previous study, we observed superior overall survival (OS) with taxane vs. ARsi in mCRPC patients positive for nuclear-localized AR-V7 protein in mCTCs
- We sought to prospectively evaluate this relationship in an independent, blinded, multicenter cross-sectional cohort

Methods
- 866 patients were selected from 4 mCRPC patients prior to initiation of ARsi or taxane at three clinical sites: Memorial Sloan-Kettering (USA), Institute of Cancer Research (UK) and the London Health Sciences Centre (Canada)
- All samples were tested with the Epic Sciences CTC test for AR-V7 nuclear protein (see below), and treatment choice was at discretion of the attending physician without knowledge of AR-V7 test result
- A risk score was developed using our previous cohort in order to adjust for possible therapy selection bias by the treating physician. The relationship between overall survival and treatment group was analyzed both in the entire cohort, and with a subset of the cohort with requisites samples from all four groups for more stringent analyses given a more balanced patient risk

Validation Cohort: 168 patient blood samples

OS of mCRPC pts by AR-V7 Status & Therapy Class

AR-V7 Predicts Therapy-Specific OS

AR-V7 Survival Consistent Across Patient Risk

OS by Baseline Risk, AR-V7 and Therapy Class

Risk Adjusted: AR-V7 Predicts Therapy-Specific OS

References

Clinical Decision Algorithm for Nuclear AR-V7 Test

Scenario 1: Risk Score Available

Discussion
1. The study results validate the clinical utility of the Epic Sciences nuclear-localized AR-V7 assay, for the context of use as a predictive biomarker to inform the choice between inhibitors or taxanes for mCRPC patients in need of a treatment change in the secondline or greater setting.
2. Patients who tested negative for nuclear AR-V7 had better OS in ARsi versus taxanes.
3. Patients who tested positive for nuclear AR-V7 had a demonstrated survival advantage when treated with taxanes.
4. In the context of second line or greater mCRPC when the decision between an ARsi versus a taxane is being considered, the utilization of the Epic Sciences nuclear-localized AR-V7 test demonstrated clinical utility as a predictive assay for overall survival

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