The detection of AR-V7 in plasma-derived exosomal RNA strongly predicts resistance to hormonal therapy in metastatic prostate cancer patients

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Introduction: Castration resistance prostate cancer (CRPC) lacks of predictive biomarkers for response and/or resistance to treatment. Recently, was found an androgen receptor splice variants (AR-V7), which is associated with resistance to hormonal therapy[1]. Nowadays, methods available for the AR-V7 analysis have substantial limitations, such as costs, difficult and long procedures or low sensitivity. Therefore, the identification of a reliable detection method may facilitate the use of this biomarker in clinical practice.

Aim: The aim of this study was to develop a new methodological approach to detect AR-V7 by digital droplet PCR in exosomal-derived RNA from plasma samples and to confirm its role as predictive biomarker of resistance to hormonal therapy in CRPC.

Patients and Methods: Thirty-six prostate cancer patients were enrolled in the present study. Plasma samples were collected before the beginning of second-line hormonal treatment (abiraterone or enzalutamide). Exosomes isolation and RNA extraction were performed and tested for analysis of AR-V7 by digital droplet PCR (BioRad®).

Results: 39% of patients were found carriers of the AR-V7 transcript. The median clinical or radiographic progression free survival was significantly longer in AR-V7 negative compared to positive patients (20 vs 3 months; P<0.001). Overall survival was significantly shorter in subjects with detectable AR-V7 at baseline compared to those with undetectable AR-V7 (8 months vs. not reached; P<0.001). In the AR-V7-positive patients, the PSA response rates was 7% (1 out of 14 men), while in the AR-V7 negative patients the PSA response rate was 64% (14 of 22 men). The AR-V7 positive subjects were more likely to be younger, Gleason Score at least 8, visceral metastases, higher PSA levels, and prior docetaxel treatment than AR-V7 negative patients.

Conclusions: The present study demonstrates that the analysis of AR-V7 on plasma-derived exosomal RNA is feasible, reproducible and sensitive. Moreover, the role of AR-V7 as a biomarker to predict resistance to hormonal therapy in CRPC is confirmed by our data, suggesting its clinical relevance.