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Analysis of AR-FL and AR-V1 in whole blood of patients with castration resistant prostate cancer as a tool for predicting response to abiraterone acetate

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Introduction & objectives: Reliable molecular diagnostic tools are still unavailable for making informed treatment decisions and monitoring the response in castration resistant prostate cancer (CRPC) patients. The aim of this study was to evaluate the significance of whole blood-circulating androgen receptor (AR) transcripts of full length (AR-FL) and splice variants (AR-Vs: AR-V1, -V3, and -V7) as biomarkers of abiraterone acetate (AA) treatment resistance in CRPC patients.

Materials & methods: After retrospective analysis in 112 prostate specimens, AR-FL, -V1, -V3, and -V7 were evaluated in 120 serial blood samples, prospectively collected from 66 CRPC patients before and during AA therapy via reverse transcription quantitative PCR. The association of AR transcript status with progression-free survival (PFS) and overall survival (OS) was assessed.

Results: In tissue analysis, significant overexpression of AR-V7 was detected in cases that subsequently developed biochemical progression (P=0.010). In blood analysis, AR-FL was present in all blood samples while AR-V1, -V3, -V7, and at least one of them was detected in 16%, 58%, 72%, and 82% of CRPC blood samples, respectively. The highest amount of AR-V1 was found in patients' blood whose response time was short (<3.0 mo) and medium (3.0-8.0 mo) in comparison to extended (>8.0 mo; P=0.004 and P=0.027, respectively). Patients having a higher level of AR-FL and/or AR-V1 had the shortest PFS (7.0 vs 12.2 mo, P=0.019). AR-V1 was an independent predictor for PFS (P<0.050), and together with AR-FL predicted OS (model's P=0.050).

Conclusion: Blood-circulating AR-FL or -V1 can serve as blood-based biomarkers to identify the primary resistance to AA and the tool to monitor *de novo* resistance development.