AR-V7 and efficacy of abiraterone and enzalutamide in men with mCRPC: Expanded analysis of the Johns Hopkins cohort


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Background: We previously reported that detection of androgen receptor variant 7 (AR-V7) mRNA in circulating tumor cells (CTCs) correlated with poor outcomes to abiraterone and enzalutamide in castration-resistant prostate cancer (CRPC) patients. Here, we expanded our cohort size to better characterize the prognostic significance of AR-V7 in this setting. Methods: We prospectively enrolled 202 CRPC patients starting abiraterone or enzalutamide, and investigated the prognostic value of CTC detection (+ vs −) and AR-V7 detection (+ vs −) using a CTC-based AR-V7 mRNA assay. We examined ≥50% PSA responses, PSA progression-free survival (PSA-PFS), clinical/radiologic progression-free survival (PFS), and overall survival (OS). We constructed multivariable models adjusting for PSA, Gleason sum, number of prior hormone therapies, prior abiraterone or enzalutamide use, prior taxane use, presence of visceral metastases, and ECOG score. We also separately examined the first-line and second-line novel hormonal therapy (NHT) settings. Results: 202 patients were enrolled (median follow-up 12.9 months, range 1.3–35.8 months). CTC+/AR-V7+ patients were more likely to have Gleason scores ≥8 (P=.05), metastatic disease at diagnosis (P=.01), higher PSA (P<.01), prior abiraterone or enzalutamide use (P=.03), prior taxane use (P=.02), and ECOG ≥1 (P=.01). Outcomes for the overall cohort (and separately for the first-line and second-line NHT cohorts) were best for CTC− patients, intermediate for CTC+/AR-V7− patients, and worse for CTC+/AR-V7+ patients. These correlations remained significant in multivariable models. Conclusions: This expanded analysis further characterizes the importance of CTC-based AR-V7 mRNA detection in predicting outcomes in CRPC patients receiving first- and second-line NHT, and is the first to suggest that the modified-AdnaTest assay should be interpreted using 3 separate prognostic categories: CTC−, CTC+/AR-V7−, and CTC+/AR-V7+.

Conflicts of Interest: ESA has served as a paid consultant/advisor for Janssen, Astellas, Sanofi, Dendreon, Essa, and Medivation; has received research funding to his institution from Janssen, Johnson & Johnson, Sanofi, Dendreon, Exelixis, Genentech, Novartis, and Tokai; and is a co-inventor of a technology that has been licensed to Tokai. JL has served as a paid consultant/advisor for Astellas, Gilead, and Sanofi; has received research funding to his institution from Orion, Mirati, Astellas, Sanofi, and Gilead; and is a co-inventor of a technology that has been licensed to Tokai.

Funding: ESA has received funding from the Prostate Cancer Foundation (YIA 2013), the Patrick C.Walsh Fund, and NIH grants R01 CA185297 and P30 CA006973. JL is currently funded by a Prostate Cancer Foundation Challenge Award, NIH grant R01 CA185297, and US Department of Defense Prostate Cancer Research Program grants W81XWH-13-2-0093 and W81XWH-15-2-0050.