Clinical Utility of Circulating Tumour Cell Androgen Receptor Splice Variant-7 Status in Metastatic Castration-resistant Prostate Cancer


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Background: Detection of androgen receptor splice variant-7 (AR-V7) mRNA in circulating tumour cells (CTCs) is associated with worse outcome in metastatic castration-resistant prostate cancer (mCRPC). However, studies rarely report comparisons with CTC counts and biopsy AR-V7 protein expression.

Methods: CTC AR-V7 status was determined for 227 peripheral blood samples, from 181 mCRPC patients with CTC counts (202 samples; 136 patients) and matched mCRPC biopsies (65 samples; 58 patients). CTC AR-V7 status was associated with clinical characteristics, CTC counts, and tissue biopsy AR-V7 protein expression. The association of CTC AR-V7 status and other baseline variables with OS was determined.

Results: Of the samples, 35% were CTC+/AR-V7+. CTC+/AR-V7+ samples had higher CellSearch CTC counts (median CTC; interquartile range [IQR]: 60, 19–184 vs 9, 2–64; Mann-Whitney test p < 0.001) and biopsy AR-V7 protein expression (median H-score, IQR: 100, 63–148 vs 15, 0–113; Mann-Whitney test p = 0.004) than CTC+/AR-V7- samples. However, both CTC- (63%) and CTC+/AR-V7- (62%) patients had detectable AR-V7 protein in contemporaneous biopsies. After accounting for baseline characteristics, there was shorter OS in CTC+/AR-V7+ patients than in CTC- patients (hazard ratio [HR] 2.13; 95% confidence interval [CI] 1.23–3.71; p = 0.02); surprisingly, there was no evidence that CTC+/AR-V7+ patients had worse OS than CTC+/AR-V7- patients (HR 1.26; 95% CI 0.73–2.17; p = 0.4). A limitation of this study was the heterogeneity of treatment received.

Conclusions: Studies reporting the prognostic relevance of CTC AR-V7 status must account for CTC counts. Discordant CTC AR-V7 results and AR-V7 protein expression in matched, same-patient biopsies are reported.
**Conflicts of interest:** AS, JCW, MBKL, DD, DNR, LP, CA, IF, JF, ZA, PR, CB, GS, RR, SM, MC, RP, AF, GF, BE, PF, AN, DB, AP, SS, AP, NT, WY, SC and JSDB are employees of The Institute of Cancer Research, which has a commercial interest in abiraterone. AS has received travel support from Roche-Genentech and speaker honorarium from Astellas Pharma. JL is an inventor of a relevant technology that has been licensed to A&G, Tokai, and Qiagen. JSDB has served as a consultant/advisory member for Astellas Pharma, AstraZeneca, Bayer, Genmab, Genentech, GlaxoSmithKline, Janssen, Medivation, Orion Pharma, Pfizer and Sanofi. JSDB is a National Institute for Health Research (NIHR) Senior Investigator. The views expressed in this article are those of the author(s) and not necessarily those of the NHS, the NIHR, or the Department of Health.

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