Clinical factors associated with AR-V7 detection in ARMOR3-SV, a randomized trial of galeterone (Gal) vs enzalutamide (Enz) in men with AR-V7+ metastatic castration-resistant prostate cancer (mCRPC).
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Journal of Clinical Oncology 2017 35:15_suppl, 5005-5005

Meeting Abstract | 2017 ASCO Annual Meeting I

GENITOURINARY (PROSTATE) CANCER

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Abstract Disclosures

Abstract

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Background: Presence of the AR-V7 splice variant may predict resistance to Enz and abiraterone in men with mCRPC. Gal is an oral agent that disrupts AR signaling via AR degradation, CYP17 lyase inhibition, and AR antagonism. ARMOR3-SV was designed to test the hypothesis that in mCRPC patients with AR-V7+ CTCs, Gal could improve radiographic progression-free survival (rPFS) versus Enz. **Methods:** In this randomized, open-label, multicenter phase 3 study (NCT02438007), men with treatment-naïve mCRPC were screened for CTC-specific AR-V7 (Qiagen), and AR-V7+ men were randomized 1:1 to Gal or Enz. rPFS (by independent blinded central review) was the primary endpoint. Planned sample size was 148, with 120 rPFS events to achieve 90% power to detect a hazard ratio of ≤0.55. **Results:** 953 patients were screened globally for AR-V7 from Sept 2015 through study closure; 73 men (8%; 95% CI 6-10%) were AR-V7+, 250 (26%) AR-V7–, and 630 (66%) had no CTCs/AR present (unevaluable). AR-V7 detection was associated with higher PSA levels (> vs < median; P < 0.01), more bone metastases (> 20 vs 11-20 vs 6-10 vs 0-5; P < 0.01), presence of M1 disease at diagnosis (dx) (yes vs no; P = 0.04), shorter time from dx to screening (< vs > median; P < 0.01), higher ECOG (≥1 vs 0; P = 0.02), prior antiandrogen use (yes vs no; P < 0.01) and prior docetaxel use (yes vs no; P < 0.01). Among the AR-V7+ men, 38 were randomized (19 Gal, 19 Enz), 31 screen failed, and 4 were discontinued from screening at study halt. Baseline characteristics were balanced. On the recommendation of the DSMB, the study was closed early as it was unlikely to meet its primary endpoint. At the time of the study closure, in the Gal and Enz arms respectively, median time on therapy was 2.0 vs 2.8 mo, median time to PSA progression (PCWG1) was 3.9 vs 3.8 mo, PSA_{50} response rates in evaluable patients were 2/16 (13%) and 8/19 (42%), and there were no new safety signals. **Conclusions:** In treatment-naïve mCRPC patients, AR-V7 detection is more common in men with higher disease burden and portends a poor prognosis. Novel study designs and alternative treatment approaches are urgently needed for AR-V7+ mCRPC patients. Clinical trial information: NCT02438007.