Evaluating Biomarkers in Metastatic Castration Resistant Prostate Cancer (mCRPC) Patients (Pts) Treated with Enzalutamide (Enza): PSA, Circulating Tumor Cell Counts, AR-V7 Status, PET Imaging vs. CT and Tc99 Scans

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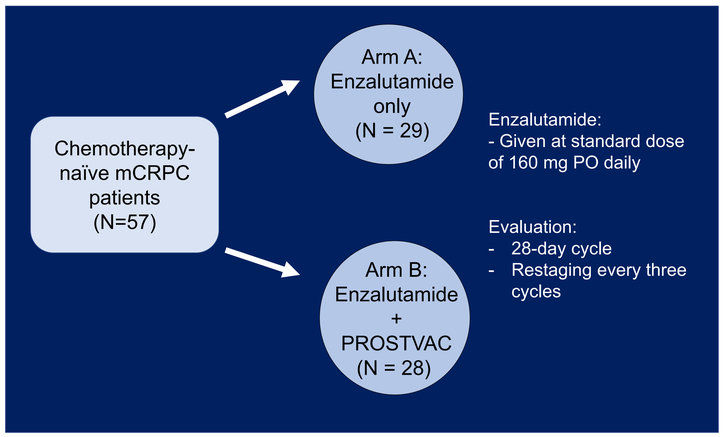
INTRODUCTION

Background: Although Prostate Cancer Working Group (PCWG) guidelines recommend continuing treatments, such as enza, for mCRPC until radiographic/clinical progression (rPD/cPD), treatment is often discontinued using other biomarkers like PSA and PET imaging.

Methods: A phase 2 trial in mCRPC randomized pts previously untreated with docetaxel, abiraterone, or enza, comparing enza +/- PROSTVAC, a therapeutic cancer vaccine. The study found no difference in progression (PD). Most pts were followed beyond PSA rise until rPD. 49 pts were analyzed for Circulating Tumor Cell (CTC) count and AR-V7 status. 18 Pts were evaluated for PD with CT/Tc99 (per PCWG) and NaF (any new lesions) every 3 months (mo). The purpose of this analysis is to determine how other biomarkers compare to rPD.

Results: 57 pts (median age 67.2 yrs and PSA 15.2) had a median follow up of 55.4 mo. 49/57 (86%) pts had rising PSA; median time to 1st PSA rise for all patients was 6.4 mo. 38/57 (67%) pts had PD (majority with rPD; 1/38 (3%) with cPD); median time to PD for all pts was 23.3 mo. In patients who experienced rPD/cPD, CTCs were detected in 11/24 (46%) samples taken at rPD vs. 3/24 (13%) samples taken at rising PSA. CTC counts were higher at rPD compared to samples taken at rising PSA (P=0.004, Wilcoxon unpaired test). 5/11 pts tested + for AR-V7 within 30 days of rPD. 18 pts had 182 paired Tc99 and NaF scans and found that 3 pts had rapid PD simultaneously on both scans, 3 pts had PD seen on NaF 54, 84, and 752 days prior to PD on Tc99 scan, and 3 pts had PD on NaF scan at 84, 85, 261 days without PD seen on Tc99 scan before off-study.

METHODS

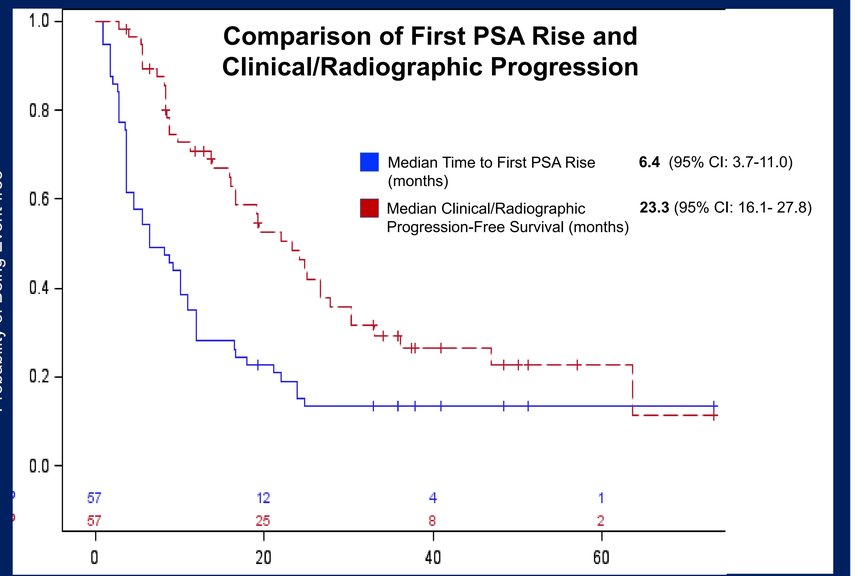


Baseline Characteristics

Total number of patients	57
Arm A (Enzalutamide only) --- no. (%) Arm B (Enzalutamide+ PROSTVAC) --- no. (%)	29 (51) 28 (49)
Age at randomization (years) Median Range	 67 (45 – 94)
Race --- no. (%) Caucasian African American Asian Multiracial	 47 (82) 7 (12) 1 (2) 2 (4)
ECOG performance status --- no. (%) 0 1	 27 (47) 30 (53)

Gleason score --- no. (%) 9-10 7-8 6	 23 (40) 29 (51) 5 (9)
PSA at baseline (ng/mL) Median Range	 15.02 (0.55 – 587.4)
Hemoglobin (g/dL) Median Range	 13 (10.4-15.5)
Alkaline phosphatase (U/L) Median Range	 91.5 (35-606)
LDH (U/L) Median Range	 178 (129-313)

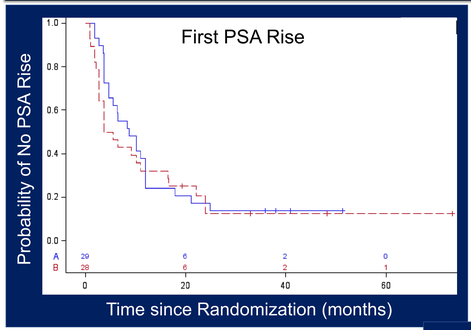
RESULTS



(Since no difference by arm, data pooled together for this analysis)

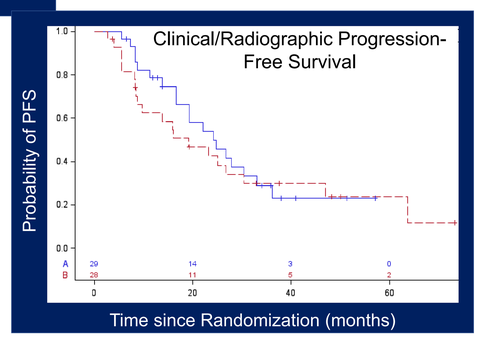
Median follow-up time (months)	**55.4**
Median PSA at progression (ng/mL) **(first of three consecutive rises)**	**1.15 (0.02 – 140.1)**
Patients still on treatment --- no. (%)	**7 (12%)**
Patients with progressive disease --- no. (%)	**38 (67%)**
Off treatment for other reasons --- no. (%)	**11 (19%)**
Death on study --- no. (%)	**1 (2%)**

Results Based on Randomization

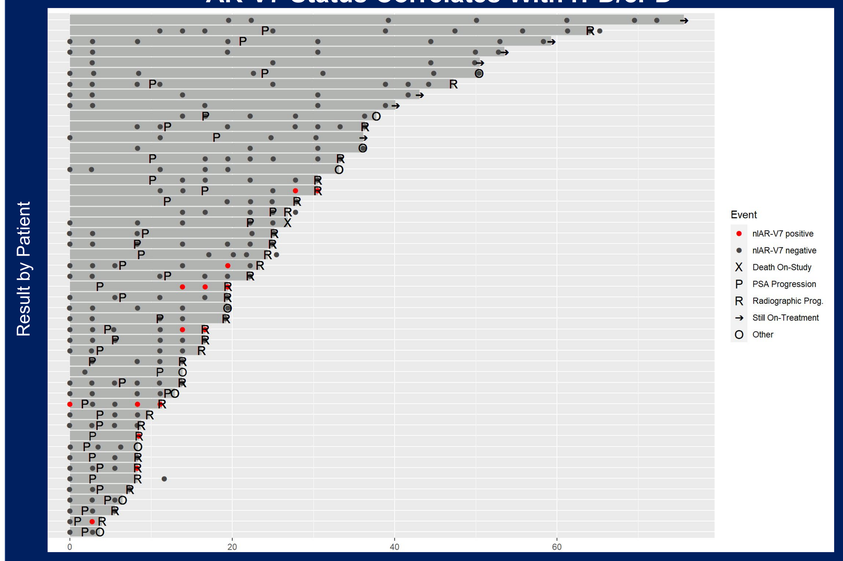


Median Time to First PSA Rise (months)
Arm A 8.7 (95% CI: 4.6 – 12.0)
Arm B 4.6 (95% CI: 2.7 – 11.0)
p=0.55

Median Clinical/Radiographic PFS (months)
Arm A 24.2 (95% CI: 16.6 – 33.1)
Arm B 19.1 (95% CI: 8.5 – 30.3)
p=0.59



AR-V7 Status Correlates With rPD/cPD



NaF PET does not appear to correlate with rPD

Patient ID	Arm	Time from Treatment Initiation to Progression in Tc99 Bone Scan (days)	Time from Treatment Initiation to Progression in NaF Scan (days)	Conclusions
3	B	81	85	PD seen almost simultaneously on NaF and Tc99
20	A	n/a	839	PD seen only on NaF
24	A	n/a	672	PD seen only on NaF
35	B	1256	504	PD seen on NaF earlier (by 752 days)
43	A	n/a	588	PD seen on NaF earlier (by 84 days)
46	A	163	169	PD seen almost simulataneously on NaF and Tc99
53	A	223	169	PD seen on NaF earlier (by 54 days)
55	A	337	252	PD seen only on NaF
57	B	580	581	PD seen almost simultaneously on NaF and Tc99

CONCLUSIONS

- This data suggests that a rising PSA or new lesions on PET imaging may not be a harbinger of near-term clinically significant disease progression in mCRPC pts treated with enza.
- The 17-month difference between the first rise in PSA and ultimate rPD/cPD seen in this analysis demonstrates the inadequacy of rising PSA as the sole marker of PD.
- PET imaging showed new lesions before Tc99 scan but with unknown clinical significance given that patients had stable Tc99 scans for 54-752 days thereafter.
- CTCs and AR-V7 status was more associated with rPD than PSA and NaF and further analysis is pending.
- This data affirms the need to be cautious with PSA and emerging biomarkers when assessing mCRPC pts treated with agents developed using PCWG criteria for rPD.

For additional information on the trial, please contact shruti.gandhy@nih.gov or madanr@mail.nih.gov

Shruti U. Gandhy has no conflicts of interest.