Evaluation of 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 evaluated 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 mos. 49/57 (86%) pts had rising PSA; median time to 1st PSA rise for all patients was 6.4 mos. 38/57 (67%) pts had PD (majority with rPD; 138/3%) with cPD); median time to PD for all pts was 23.3 mos. 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 on NaF scan at 84, 85, 261 days without PD seen on Tc99 scan before off-study.

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.