Concurrent Chemo-Hormonal Therapy of Enzalutamide (ENZ) and Cabazitaxel (CAB) in Patients (Pts) with Metastatic Castration-Resistant Prostate Cancer (mCRPC): Final Analysis of Objective Response Rate (ORR), Radiographic Progression-Free Survival (rPFS), and Overall Survival (OS)

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Background: We previously reported the PSA response rate and toxicity data of a phase 1/2 single-arm, multi-institutional trial to examine the efficacy and safety of co-administration of ENZ + CAB in mCRPC without prior chemotherapy given in the mCRPC setting. We found that full doses of ENZ (160 mg daily) and CAB (25 mg/m2) were tolerable and that 80% of pts had PSA decline ≥50%. Here, we report the final analysis of ORR, rPFS and OS.

Methods: We calculated the ORR (CR/PR) and 95% confidence intervals using the Clopper-Pearson Exact Method. We determined response according to RECIST 1.1 for measurable disease and Prostate Cancer Working Group 2 criteria for non-measurable (bone) disease. We estimated median rPFS (time from the study entry to the time of confirmed progression (radiographic or clinical) or death) and OS (time from the study entry to death) with 95% confidence intervals using the Kaplan-Meier method; data cutoff was 6/1/22. Statistical analysis was performed using R: A language and environment for statistical computing.

Results: 37 pts consented and 35 were included in the efficacy analyses (1 withdrew consent, 1 was lost to follow up before efficacy assessment); 7/35 (20%) had prior exposure to chemotherapy given for mHSPC and 9/35 (25%) had prior exposure to abiraterone (ABI), including 2/35 (25.7%) with prior exposure to chemotherapy and ABI. 28 pts had at least one on-study trial imaging study and were evaluable for ORR. After a median follow-up of 23.7 (range: 4.9 to 62.4) months (mo), median OS was 25.1 mo (95%CI 19.4 - 37.6 mo). Median PSA PFS was 11.9 mo (95%CI 9.2 - 15.4), and median rPFS was 22.2 mo (95%CI 13.6 - 25.2). PK assessments revealed that ENZ decreased CAB levels: CAB (monotherapy) Cmax 178.9ng*h/ml vs CAB (in the presence of ENZ) Cmax 85.5 ng*h/ml ($p<0.05$).

Conclusions: The combination of ENZ+CAB in this heterogeneous mCRPC population, which included about a quarter of pts with prior chemotherapy and ABI exposure, resulted in an OS of 22.5 mo comparing favorably with the OS of 25.2 mo seen in the FIRSTANA trial of single agent CAB in docetaxel naïve men, 15.1 mo post chemotherapy in the TROPIC trial, and 13.6 mo in the post-docetaxel, post-ABI in the CARD trial. Of note, the rPFS in this trial was 22.2 months compared to 5.1 months in FIRSTANA suggesting

improved efficacy; however cross-trial comparisons are discouraged due to several confounders. Chemo-hormonal therapies and prognostic/predictive biomarkers warrant further study in mCRPC. Clinical trial information: NCT02522715.

Radiographic Best Response (n=28)	Pts N (%)	Lower 95%CI	Upper 95%CI
Complete response	3 (10.7%)	2.3%	28.2%
Partial response	11 (39.3%)	21.5%	59.4%
Stable disease	12 (42.9%)	24.5%	62.8%
Progressive disease	2 (7.1%)	0.9%	23.5%
ORR	**14 (50%)**	**30.6%**	**69.4%**

Funding Acknowledgement:

AOS: W81XWH2220021; NIH T32 Training in Cancer Biology and Transplantation Training Grant 5T32CA009515-33; Fellowship; Prostate Cancer Foundation Young Investigator Award, Pacific Northwest Prostate Cancer SPORE CA097186; Pacific Northwest Prostate Cancer SPORE CA097186 Pilot Grant; Univ. of Washington, Canary Foundation, Movember Foundation.

HCC: Institute for Prostate Cancer Research, Advancing Cancer Treatment,
Pacific Northwest Prostate Cancer SPORE CA097186
Prostate Cancer Foundation Awards
Congressional Designated Medical Research Program (CDMRP) awards PC131820, W81XWH-15-1-0430, W81XWH-17-2-0043
Medical Oncology Training Grant 5T32CA009515-33
RedCap: This publication was supported by the National Center For Advancing Translational Sciences of the National Institutes of Health under Award Number UL1 TR002319.

JG: 1R01CA275055-01A1; W81XWH2220021

Conflict of Interest:

AOS: Travel funds from Astra Zeneca, Consulting for AstraZeneca, Lantheus, DSMC for AstraZeneca. Institutional funding for research from Arvinas, U.S., Curium, ESSA Pharma, Prostate Cancer Foundation, Novartis Pharmaceuticals Corporation, Arvinas Androgen Receptor Inc, Accutar Biotechnology Inc., Janux Therapeutics, OncoC4, AstraZeneca LP, Pfizer Inc, Regeneron Pharmaceuticals Inc.

HHC: Research funds to institution from Clovis Oncology, Color Genomics, Janssen, Medivation, Promontory Pharmaceutics, Sanofi; Consulting for AstraZeneca

JG: institutional funding for research from Merck, Sanofi, Janssen, and Curium.