Comprehensive Genomic Profiling of Black and non-Hispanic White Men with Prostate Cancer

Sharon H. Choi[1], Tolulope Adeyelu[2], Andrew Elliott[2], Brent Rose[1], Aditya Bagrodia[1], Tyler Seibert[1], Neeraj Agarwal[3], Oliver Sartor[4], Norm Smith[2], Pedro Barata[5], Rana R. McKay[1]

[1]University of California San Diego, La Jolla, CA, [2]Caris Life Sciences, Phoenix, AZ, [3]University of Utah, Salt Lake City, UT, [4]Mayo Clinic, Rochester, MN, [5]Seidman Cancer Center, Cleveland OH

Abstract #5022

INTRODUCTION

- Racial disparities are evident in prostate cancer (PCa), with Black men experiencing a higher incidence and worse survival compared to non-Hispanic White (NHW) patients.
- The molecular alterations that distinguish these groups remain incompletely characterized.
- Herein, we investigate the clinical-genomic features that potentially contribute to the differences in outcomes between Black and NHW patients with PCa.

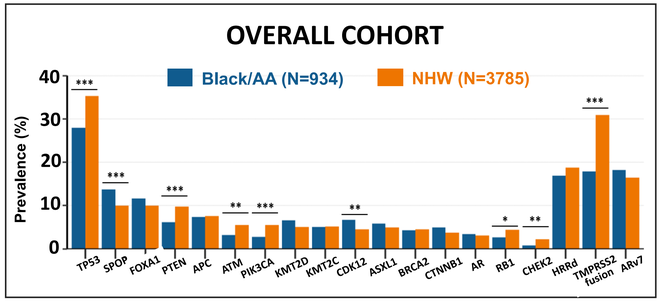
METHODS

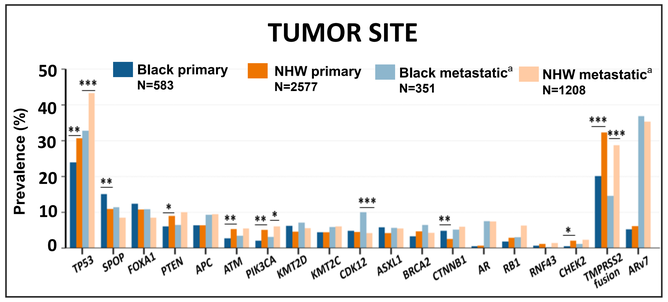
- Comprehensive next-generation sequencing of DNA (592-gene panel/whole exome) and RNA (whole transcriptome) was performed at Caris Life Sciences on PCa tissue samples collected from 2015 to 2023. PCa tissue was derived from primary prostatic and/or metastatic sites. Analysis was limited to samples diagnosed as prostate adenocarcinoma.
- Transcriptomic gene signatures, including Androgen Receptor (AR) signaling and Neuroendocrine PCa (NEPC) scores, were calculated.
- Castration-sensitive PCa (CSPC) was defined as specimen collected ≤ 90 days after ADT initiation; Castration-resistant PCa (CRPC) was defined as specimen collected > 90 days after ADT initiation.
- Real-world overall survival (OS) data was obtained from insurance claims and was analyzed using Kaplan-Meier estimation.

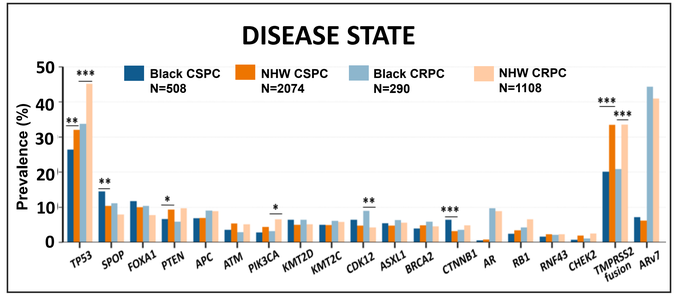
BASELINE CHARACTERISTICS

		Black/AA (N= 1078)	NHW (N= 4334)	*p*-value
Median age (range)		66 (36–89)	71 (35–89)	**<0.001**
Specimen Sites no. (%)	Prostate	619 (57%)	2709 (63%)	
	Lymph Node	146 (14%)	474 (11%)	
	Bone	96 (9%)	351 (8%)	
	Genitourinary	60 (6%)	282 (7%)	
	Liver	56 (5%)	239 (6%)	**0.014**
	Gastrointestinal	27 (3%)	75 (2%)	
	Lung	23 (2%)	98 (2%)	
	CNS	22 (2%)	42 (1%)	
	Other	29 (3%)	64 (1%)	
Histology	Adenocarcinoma	1066 (99%)	4242 (98%)	
	Neuroendocrine	2 (0.18%)	35 (1%)	0.453
	Mixed Histology	10 (0.92%)	57 (1%)	
Disease State	CSPC	603 (66%)	2381 (67%)	0.504
	CRPC	307 (34%)	1150 (33%)	

Frequency of Somatic Alterations by Race

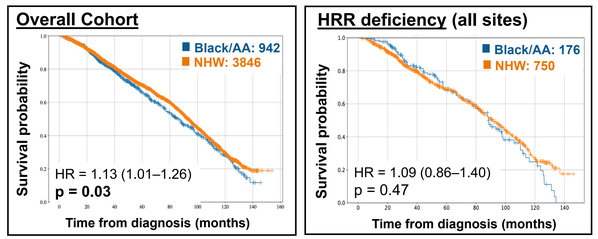


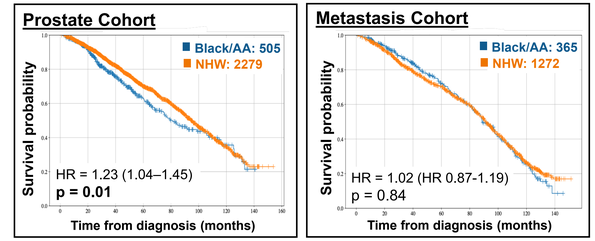


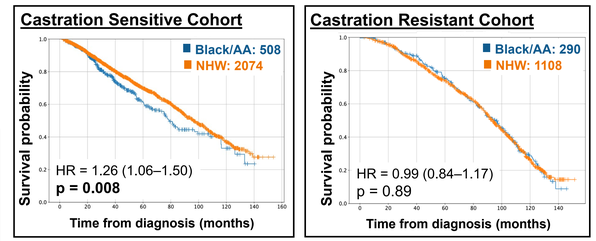


[a] Metastatic sites exclude bladder, kidney, ureter, and urethra. HRRd (homologous recombination repair deficiency) defined as alterations in *BRCA1, BRCA2, ATM, CDK12, CHEK1, CHEK2, FANCA, FANCL, PALB2, RAD51C*, or *RAD51D*. AA= African American.
*p<0.05, **p <0.01, ***p <0.001

OS between Black and NHW patients

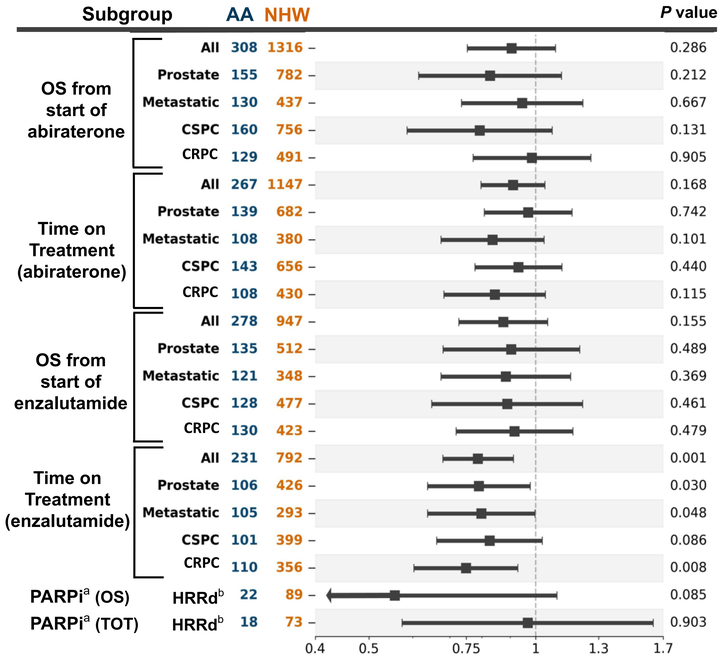






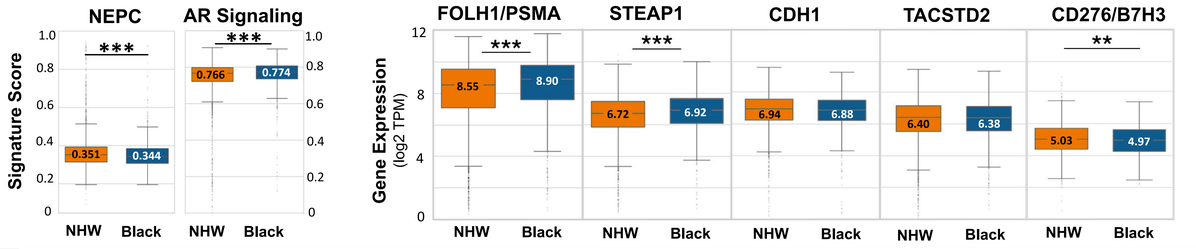
Metastasis cohort excludes bladder, kidney, ureter, and urethra. OS was measured from date of diagnosis to death or last follow up. AA = African American

Association between OS/TOT and Race



Hazard ratios for OS and time on treatment (TOT) in selected treatment subgroups were estimated using univariate Cox regression models to compare outcomes between the two racial groups. TOT was calculated from start to finish of treatment. [a] PARP inhibitor (PARPi) included niraparib, olaparib, rucaparib, and talazoparib. [b] HRRd (homologous recombination repair deficiency) defined as alterations in *BRCA1, BRCA2, ATM, CDK12, CHEK1, CHEK2, FANCA, FANCL, PALB2, RAD51C*, or *RAD51D*.

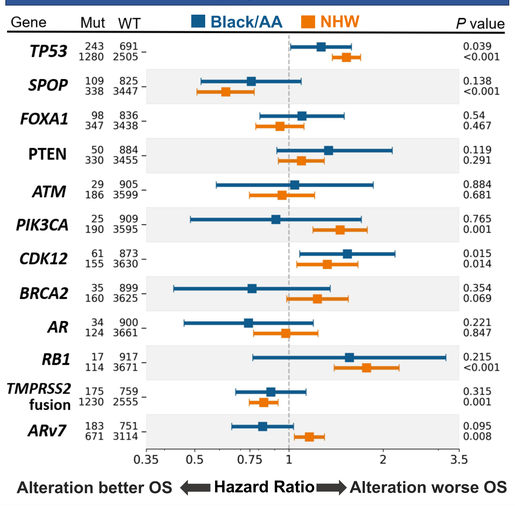
Transcriptomic Differences in Tumors by Race (Overall Cohort)



KEY TAKEAWAYS/CONCLUSIONS

- Prostate cancer tumors from Black/AA patients exhibit a distinct genomic profile characterized by a lower frequency of alterations in *TP53*, *PTEN*, *PIK3CA*, *RB1*, and *CHEK2;* fewer *TMPRSS2* fusions, and a higher prevalence of *SPOP* and *CDK12* alterations in the overall cohort.
- Among CRPC tumors, *TP53* alterations were more common in NHW men, while *CDK12* mutations were more frequent in tumors from Black patients.
- Tumors from Black patients had higher *FOLH1/PSMA* and *STEAP1* expression, elevated AR scores, but lower *CD276/B7H3* expression and NEPC scores.
- Black patients had a significantly longer duration of treatment with enzalutamide in both the CSPC and CRPC subgroups.
- Despite having molecular features associated with better prognosis, Black men demonstrated worse survival outcomes, pointing to multifaceted determinants of disease outcomes.
- These findings highlight genomic differences in diverse prostate cancer populations and suggest therapeutic opportunities to address outcome disparities.

OS stratified by genetic alterations



@DrRanaMcKay

References: 1. Mahal et al., *N Engl J Med* 2020; 383:1083-1085. 2. Siegel et al., *CA Cancer J Clin* 2024; 74:12-49. 3. Lowder et al., *Cancer Lett* 2022; 531:71-82. 3. Riviere et al., *Cancer* 2020; 126:1683-1690. 5. Koga et al., *Clin Cancer Res* 2020; 26:4651-4660. 6. George et al., *Cancer* 2021; 127:2954-2965.