# *CDK12* Pathogenic Mutations in African American and White Patients with Prostate Cancer

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## INTRODUCTION

- African American men are underrepresented in prostate cancer (PC) trials but have a greater probability of developing and dying from PC than other race populations.
- *CDK12* mutations in PC are associated with aggressive disease, increased metastasis, and decreased overall survival.
- This study reports data from next-generation sequencing (NGS) of tissue from a real-world dataset of patients with PC to investigate the frequency of pathogenic *CDK12* mutations in African American men and White men.

## METHODS

Primary PC Patients (N = 3,026) + Molecular profiling with Tempus xT assay*

*Exclusion Criteria:*
- Microsatellite Instability high (MSI-H)
- Tumor Mutational Burden (TMB) ≥10
- Mismatch Repair deficient (MMR-d).

Retrospective review of de-identified patient data

Chi-square and Fischer's Exact tests were used where appropriate to compare alterations between AA and White patients

- **Frequency and types of pathogenic *CDK12* mutations**
- **Co-mutation in other assessed genes**

Corrections for multiple testing were also applied.

*Tempus xT assay - solid tumor, 648 genes, 500× coverage, full transcriptome RNAseq for a subset of patients

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## SUMMARY


- African American men with prostate cancer show a **higher frequency of pathogenic *CDK12* mutations** than White men in a large real-world population.
- Co-mutations did not vary by race, and the alterations were most likely to be truncating mutations in both races.


## RESULTS

**Table 1.** *Cohort Characteristics.*

| | Overall, N = 3,026[1] | White, N = 2,444[1] | Black or African American, N = 582[1] |
|---|---|---|---|
| **Age at Diagnosis** | 65 (60, 72) | 66 (60, 73) | 63 (58, 68) |
| Unknown | 439 | 354 | 85 |
| **Ethnicity** | | | |
| Not Hispanic or Latino | 1,365 (97%) | 1,147 (97%) | 218 (98%) |
| Hispanic or Latino | 45 (3.2%) | 41 (3.5%) | 4 (1.8%) |
| Unknown | 1,616 | 1,256 | 360 |
| **Stage** | | | |
| Stage 4 | 1,511 (92%) | 1,207 (92%) | 304 (94%) |
| Stage 3 | 88 (5.4%) | 73 (5.6%) | 15 (4.6%) |
| Stage 2 | 38 (2.3%) | 32 (2.4%) | 6 (1.8%) |
| Stage 1 | 3 (0.2%) | 3 (0.2%) | 0 (0%) |
| Unknown | 1,386 | 1,129 | 257 |
| Advanced stage | 1,921 (63%) | 1,541 (63%) | 380 (65%) |
| **Tissue site** | | | |
| Prostate | 1,935 (64%) | 1,558 (64%) | 377 (65%) |
| Other site | 1,091 (36%) | 886 (36%) | 205 (35%) |

[1] Median (IQR); n (%)

[2] Wilcoxon rank sum test; Pearson's Chi-squared test; Fisher's exact test

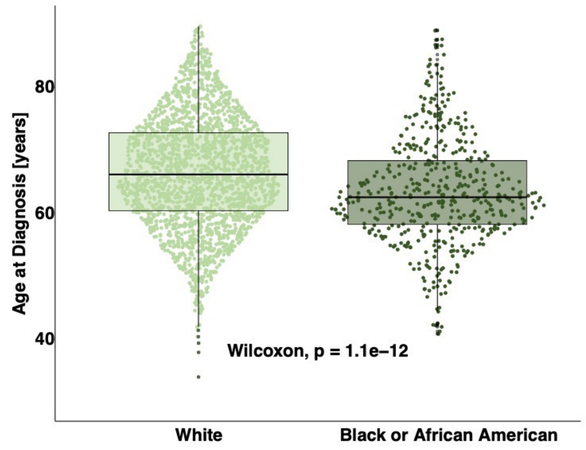


**Figure 1.** *Age at Diagnosis.*
582 African American and 2,444 White patients were included. African American were younger at diagnosis than Whites (median 63 vs 66 years; p<0.001).

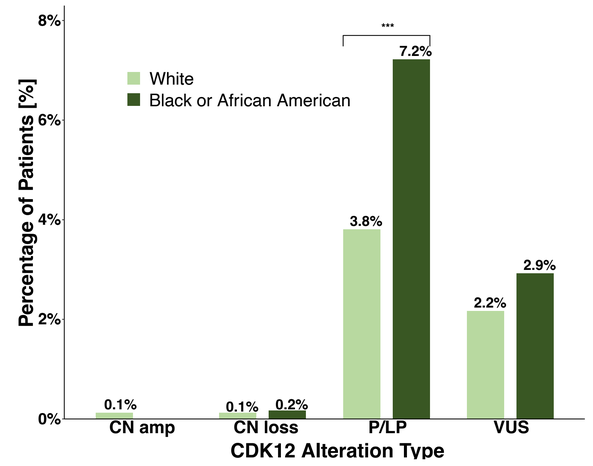


**Figure 2.** *CDK12 Alteration Types.*
Tissue samples from African American men were significantly more likely than those from Whites to express a pathogenic *CDK12* mutation (42 [7.2%] vs 93 [3.8%], p<0.001).

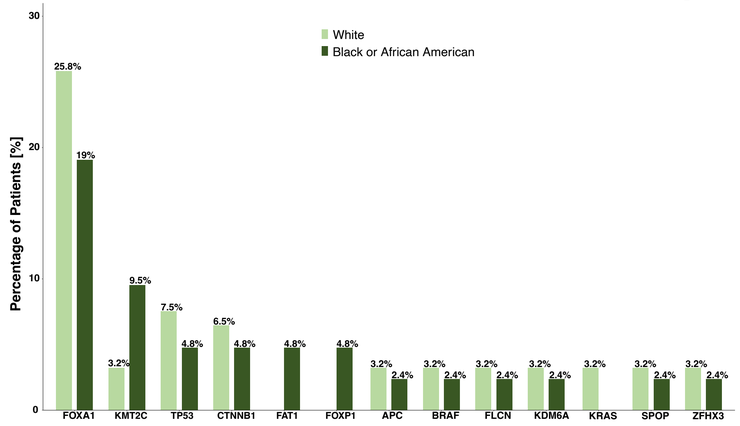


**Figure 3.** *Short variant P/LP alterations found in 3% or more of the CDK12 altered population.*
Most of the variants identified were truncating mutations. There were no differences in truncating vs. non-truncating alterations between White and African American men. There were no differences in the prevalence or distribution of co-mutations between the two populations.

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