Prognostic Relevance of Aurora Kinase A (*AURKA*) Expression in Prostate Cancer (PCa)

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INTRODUCTION

Amplification and overexpression of the *AURKA* gene characterize aggressive variants of prostate cancer, such as castration-resistant (CR) PCa and neuroendocrine PCa (NEPC), representing both a marker of progression and a promising therapeutic target.

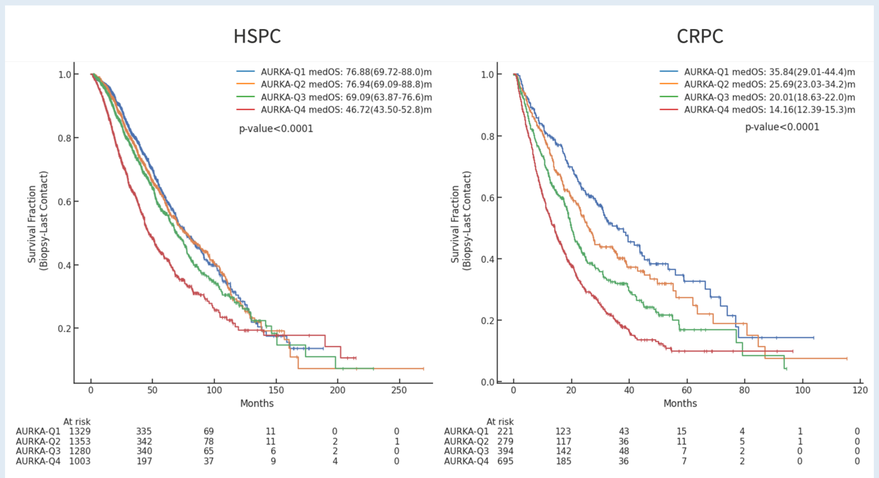
METHODS

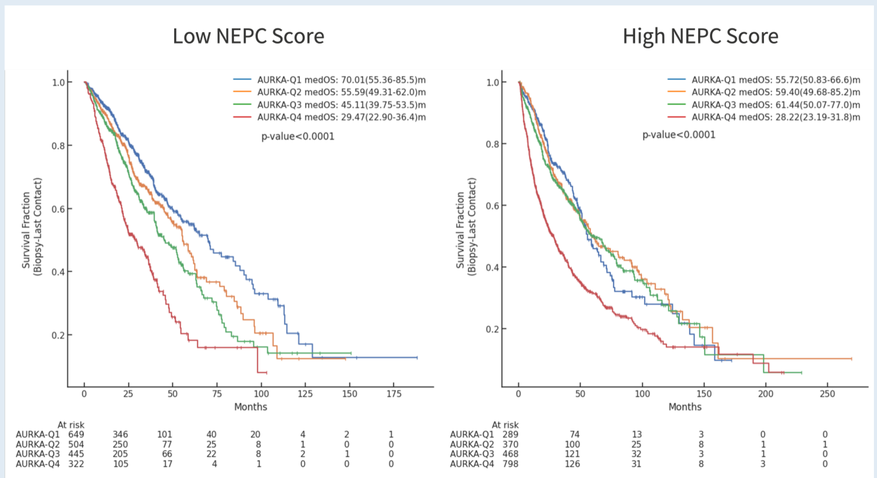
- 7755 Prostate Cancer specimens were sequenced for DNA and RNA at Caris Life Sciences
- Castrate status was defined as HSPC if specimen was collected having not undergone any ADT (ADT-naïve) or if it was collected within 90 days from the initiation of any ADT (ADT-sensitive). Specimens were considered CRPC if they were collected after 90 days from the initiation of any ADT.
- Specimens were considered as primary or metastatic based on their sites of biopsy
- Specimens were grouped quartiles based on *AURKA* RNA expression. AR and NEPC scores were calculated as previously reported. Specimens were categorized into AR Score-H/L or NEPC Score-H/L based on the highest and lowest quartiles of each score respectively.
- Real-world overall survival information was obtained from insurance claims data, and Kaplan–Meier estimates were calculated from specimen collection to last clinical contact. Hazard ratios (HR) and p-values were calculated using the Cox proportional hazards model and the log-rank test, respectively.

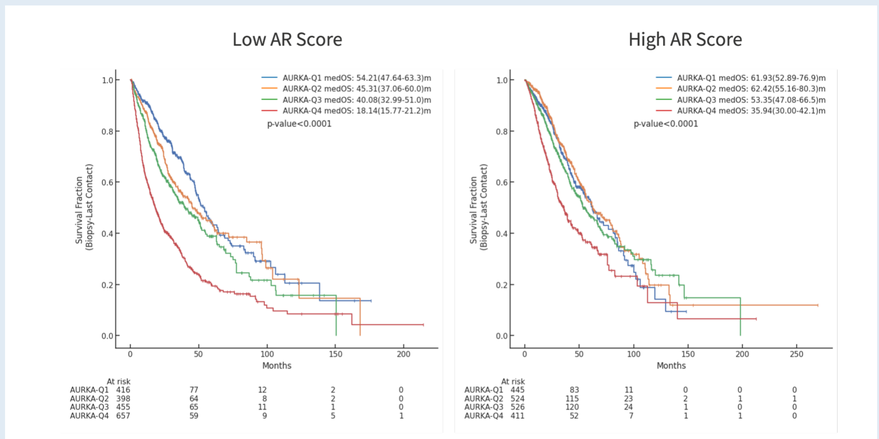
RESULTS	
Conditions	**HR (95% CI)**
White	2.6 (2.3-2.9)
Black/AA	1.9 (1.5-2.5)
non-Hispanic/Latino	2.6 (2.3-2.9)
Hispanic/Latino	2.3 (1.7-3.2)
Primary	1.7 (1.5-2)
Metastatic	2 (1.7-2.4)
NEPC-L	2.3 (1.7-3.1)
NEPC-H/AR-L	2.1 (1.6-2.8)
CS	1.9 (1.6-2.2)
CR	2.4 (2-3)

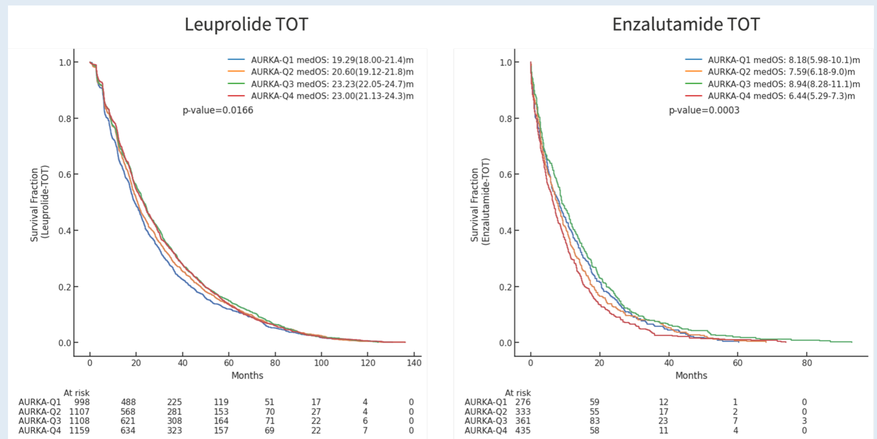
Table 1: HR comparing OS in Q4 vs Q1 (all p<0.0001)

ANALYSIS









RESULTS

- Compared to Q1, Q4 was associated with a higher median age (69 vs 67 years) and a higher proportion of non-Hispanic/Latinos (75 vs 70%), NEPC-H (42 vs 15%), metastatic (60 vs 22%), CR (46 vs 20%, all q<0.05) disease. *Q4* was also associated with poor prognosis independent of race and ethnic backgrounds.
- Despite the significant enrichment of aggressive disease, *Q4* was associated with poor prognosis independent of metastatic, NEPC-L or castration status. Further within NEPC-H specimens, *Q4* was prognostic only among those that were also AR-L (Table 1).
- Relative to Q1, Q4 samples were enriched for mutations in *TP53* (48 vs 23%), *RB1* (10 vs 1%) and *PTEN* (11 vs 7%, all q<0.05). Interestingly, *Q4* was associated with a longer Leuprolide-TOT (HR: 0.9(0.8-0.97), p<0.01) and a shorter Enzalutamide-TOT (HR: 1.2 (1-1.4), p<0.05)

CONCLUSION

- Analysis of a large dataset revealed that high AURKA expression correlates with poor prognosis across clinical and demographic subpopulations.
- AURKA inhibitors might enhance outcomes of metastatic PCa treated with AR pathway inhibitors by intensifying AR inhibition, increasing DNA-damage-related cell death, and/or preventing escape mechanisms like NEPC. Further studies are needed to identify contexts where AURKA inhibitors can improve metastatic PCa outcomes.