

Conference Abstracts

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Treatment and outcomes among patients with mCRPC with an AR gene alteration: Analysis from the Kaiser Permanente Northern California Healthcare System.

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Abstract

Background

Androgen receptor gene alterations (mutAR) are a major mechanism of resistance in metastatic castration-resistant prostate cancer (mCRPC), most commonly emerging after exposure to novel hormonal agents (NHA). Optimal treatment for patients with mutAR remains uncertain. Current NCCN guidelines recommend continued androgen deprivation therapy (ADT) with sequential use of NHAs or non-NHA therapies, including taxane chemotherapy, PARP inhibitors, immunotherapy, and lutetium-177–PSMA-617 in selected patients. We evaluated real-world outcomes of patients with mutAR treated within an integrated healthcare system.

Methods

We retrospectively identified 75 patients with mCRPC and mutAR from 2,884 patients with advanced prostate cancer who underwent tumor next-generation sequencing in the Kaiser Permanente Northern California (KPNC) health system between November 2017 and July 2026. Demographic characteristics, treatments for metastatic castration-sensitive and castration-resistant disease, progression-free survival (PFS), and overall survival (OS) were collected. Primary

endpoints were PFS on first- and second-line CRPC therapy. Secondary endpoints included PFS and OS with NHA- versus non-NHA-based treatment.

Results

Median age was 72 years (range, 44–93). AR amplification was the most common alteration (75%), followed by the AR H875 ligand-binding domain mutation (14.7%). TP53 (52%), PTEN (32%), and CCND1 (12%) were the most frequent co-mutations. Median PFS was 11 months with first-line and 5 months with second-line CRPC therapy. In the first-line setting, 59 patients received ADT plus NHA and 16 received ADT plus non-NHA therapy. Median PFS was 13 versus 5 months, respectively. In the second-line setting, median PFS was 6 versus 4 months. Median OS for the cohort was 35.1 months (95% CI, 23.8–51.2), with OS of 46.7 months for ADT plus NHA versus 20.7 months for ADT plus non-NHA therapy.

Conclusion

In this real-world KPNC cohort, AR amplification was the predominant AR alteration. First-line NHA-based therapy was associated with longer PFS and OS than non-NHA therapy, although outcomes declined substantially with

subsequent therapy, highlighting the need for more effective treatment strategies.

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