Talazoparib Plus Enzalutamide in Patients With *HRR*-Deficient mCRPC: Practical Implementation Steps for Oncology Nurses and Advanced Practice Providers

Jennifer Lloyd, MSN, FNP-C, AOCNP®, Nazy Zomorodian, MSN, CUNP, CCRC, Geeta Devgan, PhD, and Julia Batten, ANP-BC, MSN, MPH

BACKGROUND: About one-quarter of patients with advanced prostate cancer have alterations in homologous recombination repair (*HRR*) genes. In a global phase 3 study, talazoparib plus enzalutamide significantly improved progression-free survival in patients with *HRR*-deficient metastatic castration-resistant prostate cancer (mCRPC).

OBJECTIVES: This article reviews the role of oncology nurses and advanced practice providers (APPs) in administering talazoparib plus enzalutamide in patients with mCRPC.

METHODS: This review and hypothetical case study illustrate the role of oncology nurses and APPs in the administration of talazoparib plus enzalutamide and the management of adverse events to ensure safe and effective use in clinical practice.

FINDINGS: Oncology nurses and APPs play an important role in the dosing and administration of talazoparib plus enzalutamide and can recognize and manage adverse events in patients with *HRR*-deficient mCRPC.

KEYWORDS
talazoparib; enzalutamide; mCRPC; treatment management; adverse events

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PROSTATE CANCER IS THE SECOND MOST PREVALENT MALIGNANCY in men, with an estimated 299,010 new cases and 35,250 deaths predicted across the United States in 2024 (Siegel et al., 2024; Sung et al., 2021). North America has one of the highest incidence rates for prostate cancer in the world at 109.9 cases per 100,000 people, with a high racial disparity in the United States; mortality rates in Black men are about two to four times higher than those in every other racial and ethnic group (Siegel et al., 2023; Sung et al., 2021). In addition, following two decades of decline, the incidence of prostate cancer increased annually by 3% between 2014 and 2019, the equivalent of 99,000 new cases, which was driven by an increase in patients diagnosed with higher-grade disease (Borregales et al., 2022; Siegel et al., 2023). Despite research efforts, the etiology of prostate cancer is limited to advanced age, family history, and genetic biomarkers as established risk factors (Sung et al., 2021).

About one-quarter of patients with advanced prostate cancer have alterations in homologous recombination repair (*HRR*) genes, including *BRCA1*/*BRCA2*, in their tumors (Chung et al., 2019), which can lead to increased genomic instability and potential sensitivity to biomarker-targeted therapies such as poly(ADP-ribose) polymerase (PARP) inhibitors (Jiang et al., 2021; Lord & Ashworth, 2017; Zhang et al., 2020). Of the *HRR* genes, PARP inhibitors have shown higher efficacy in tumors harboring *BRCA1*/*BRCA2* alterations than in those without (Faraoni & Graziani, 2018). PARP inhibitors trap PARP1 and PARP2 on DNA lesions, resulting in an accumulation of DNA double-strand breaks and eventual cell death (Boussios et al., 2020; Javle & Curtin, 2011). Preclinical evidence suggests interplay between the androgen receptor, which largely drives the growth of prostate cancer cells, and PARP (Agarwal, Zhang, et al., 2023; Asim et al., 2017; Li et al., 2017). Agarwal, Zhang, et al. (2023) describe additional details on the molecular activity of PARP inhibitors with androgen receptor pathway inhibitors. Based on results from the phase 3 TALAPRO-2, PROpel, and MAGNITUDE trials, PARP inhibitors in combination with androgen receptor pathway inhibitors have demonstrated synergistic antitumor benefits (Agarwal, Azad, et al., 2023; Chi et al., 2023; Clarke et al., 2022) and have been approved in the United States