



Positive Quality Intervention: Talazoparib (Talzenna®) and Enzalutamide (Xtandi®) in HRR Gene-Mutated Metastatic Castration-Resistant Prostate Cancer

Description: This document will help in the initiation and management of patients taking talazoparib in combination with enzalutamide for HRR gene-mutated metastatic castration-resistant prostate cancer.

Background: Talazoparib is a PARP inhibitor indicated in combination with enzalutamide for the treatment of adult patients with homologous recombination repair gene-mutated (HRRm) metastatic castration-resistant prostate cancer (mCRPC) and as a single agent, for the treatment of adult patients with deleterious or suspected deleterious germline BRCA-mutated (gBRCAm) HER2-negative locally advanced or metastatic breast cancer.^{1,2} HRRm include BRCA1, BRCA2, ATM, ATR, CDK12, CHEK2, FANCA, MLH1, MRE11A, NBN, PALB2, or RAD51C. The phase 3 TALAPRO-2 study investigated combining the poly(ADP-ribose) polymerase (PARP) inhibitor talazoparib with enzalutamide versus enzalutamide alone as first-line treatment of mCRPC. The primary endpoint, radiographic progression-free survival, was met at the time of the analysis for the talazoparib group was at least 21.9 months (median not reached) vs 13.8 months for the placebo group (hazard ratio (HR) 0.45; 95% confidence interval (CI), 0.33-0.61; $P < 0.0001$). Data for overall survival are immature but favor talazoparib (HR 0.69; 95% confidence interval, 0.46-1.03; $P = 0.07$).³ NCCN Guidelines have designated this combination as category 1 preferred for patients with no prior docetaxel/no prior novel hormone therapy with HRRm, category 2B in patients with prior novel hormone therapy/no docetaxel with HRRm, and category 2A for patients with prior docetaxel/no prior novel hormone therapy with HRRm.⁴

PQI Process: Identify patients with HRR gene-mutated mCRPC or test for germline and somatic gene mutations if not yet done; upon receipt of a new prescription for talazoparib in combination with enzalutamide

- Verify initial dosing for talazoparib 0.5 mg by mouth once daily
- Ensure orders for enzalutamide 160 mg by mouth once daily
- Ensure orders for gonadotropin releasing hormone (GnRH) analog or bilateral orchiectomy
- Nausea/decreased appetite are common adverse effects, but typically seen at Grade 1/2 (low emetic potential)
- Dose interruption may be an effective method for the management of anemia, neutropenia, decreased platelet count, and fatigue
- Dose modifications
 - Monitor for pancytopenia (particularly anemia) monthly; if hematologic toxicities do not resolve within 28 days, discontinue and refer for hematologist consultation for assessment of Myelodysplastic Syndrome (MDS)/Acute Myelogenous Leukemia (AML), discontinue if MDS/AML is confirmed (0.4% in TALAPRO-2)
 - Renal impairment
 - Moderate renal impairment (CrCl 30 - 59 mL/min) decrease talazoparib to 0.35 mg orally once daily
 - Severe renal impairment (CrCl 15 - 29 mL/min) decrease talazoparib to 0.25 mg orally once daily
 - The effect of coadministration of P-gp inhibitors on talazoparib in combination with enzalutamide has not been studied; monitor patients for increased adverse reactions and modify the dosage as recommended for adverse reactions
 - BCRP Inhibitors: Monitor for potential increased adverse reactions
- Withhold the start of talazoparib until patients have adequately recovered from any previous hematologic toxicity

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Adverse Reactions	Withhold talazoparib Until Levels Resolve To	Resume talazoparib
Hemoglobin < 8 g/dL	≥ 9 g/dL	Resume talazoparib at a reduced dose
Platelet count < 50,000/μL	≥ 75,000/μL	
Neutrophil count < 1,000/μL	≥ 1500/μL	
Non-hematologic Grade 3 or 4	≤ Grade 1	Consider resuming talazoparib at a reduced dose or discontinue

Dose Reductions	Dose Level
Recommended starting dose	0.5 mg by mouth once daily
First dose reduction	0.35 mg by mouth once daily
Second dose reduction	0.25 mg by mouth once daily
Third dose reduction	0.1 mg by mouth once daily

Patient-Centered Activities:

- Provide talazoparib [Oral Chemotherapy Education \(OCE\)](#) sheet and enzalutamide [OCE](#) sheet
- Review side effects of fatigue, nausea/vomiting, headache, and anemia with patient/family
- Ensure the patient is aware of the need for monthly laboratory monitoring
- Can be taken with or without food, at the same time once a day, do not crush/break capsule
- Advise male patients with female partners of reproductive potential and pregnant partners to use effective contraception during treatment and for 4 months following the last dose
- Patient Assistance: [NCODA Financial Assistance Tool](#)

References:

1. [Talzena® \(talazoparib\) Prescribing Information.](#)
2. [Xtandi® \(enzalutamide\) Prescribing Information.](#)
3. Fizazi K, Azad AA, Matsubara N, et al. First-line talazoparib with enzalutamide in HRR-deficient metastatic castration-resistant prostate cancer: the phase 3 TALAPRO-2 trial. *Nature Medicine*. 2024;30(1):257-264. doi:https://doi.org/10.1038/s41591-023-02704-x.
4. NCCN Guidelines Prostate Cancer. Nccn.org. Published 2024 https://www.nccn.org/professionals/physician_gls/pdf/prostate.pdf.