

PARP Inhibitors in Advanced Prostate Cancer: Molecular Testing and Treatment at a Glance

Overview

Genomic alterations (both germline and somatic/tumor) in DNA damage repair genes, including those involved in HRR, occur in patients with prostate cancer¹

- Localized disease: approximately 1 in 20 men
- Metastatic disease: approximately 1 in 4 men
- *BRCA2* alterations are the most common (other identified alterations include *BRCA1*, *CDK12*, *CHEK1/2*, *PALB2*, and more)

HRR-deficient cells are sensitive to PARP inhibitors



Molecular Diagnostic Testing

Multiple guidelines are available that include molecular testing recommendations for patients with prostate cancer

Organization	Guideline Link
European Society for Medical Oncology	esmo.org/guidelines/guidelines-by-topic/esmo-clinical-practice-guidelines-genitourinary-cancers/clinical-practice-guidelines-prostate-cancer
European Association of Urology	uroweb.org/guidelines/prostate-cancer
National Comprehensive Cancer Network	nccn.org/guidelines/guidelines-detail?category=1&id=1459
American Urological Association	auanet.org/guidelines-and-quality/guidelines/advanced-prostate-cancer

Germline testing of blood/saliva for HRRm can inform patient prognosis, as well as potential disease risk and screening options for family members

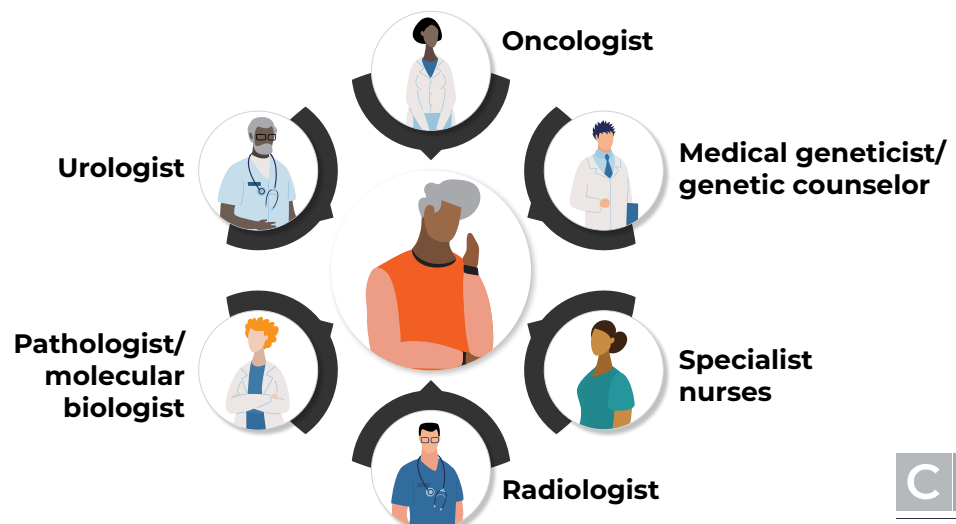
Tumor/somatic tissue testing can inform treatment decisions and patient prognosis, as well as identify alterations of potential germline origin

Both somatic and germline testing for HRRm are important for patients diagnosed with metastatic prostate cancer—one does not replace the other

Refer to specific guidelines for information and recommendations on:

- Gene panels and NGS platforms
- HRR genes to be assessed
- When during the disease course to test for HRRm
- Use of various tumor sample types (eg, surgical, biopsy, archival, ctDNA)

A multidisciplinary team (in person or virtual) may help with establishing processes, review of testing results, and analysis of therapeutic implications



Treatment With PARP Inhibitors



Patients with **mCRPC** may be eligible for treatment with an approved PARP inhibitor



Patients with **mHSPC** may be eligible for ongoing trials evaluating PARP inhibitors

PARP Inhibitor Approvals in mCRPC (May 2024)

FDA-Approved Indication²

Patients with **HRR-mutated mCRPC** who have progressed on prior enzalutamide or abiraterone acetate for metastatic disease or CRPC

Monotherapy²⁻⁴

Olaparib

EMA-Approved Indication³

Patients with **BRCA-mutated mCRPC** who have progressed on a prior NHA for metastatic disease or CRPC

FDA-Approved Indication⁴

Patients with **BRCA-mutated mCRPC** who have progressed on AR-directed therapy *and* a taxane

Rucaparib



✔ Treatment should continue **until progression or unacceptable toxicity**²⁻⁴

✔ An LHRH analogue should be continued in patients who are not surgically castrated^{2,3}

FDA-Approved Indication²

In combination with abiraterone and prednisone or prednisolone for the treatment of adult patients with **deleterious or suspected deleterious BRCA-mutated mCRPC**

Combination Therapy^{2,3,5-8}

Olaparib

EMA-Approved Indication³

In combination with abiraterone and prednisone or prednisolone for the treatment of adult patients with **mCRPC in whom chemotherapy is not clinically indicated**

FDA-Approved Indication⁵

In combination with prednisone for the treatment of adult patients with **deleterious or suspected deleterious BRCA-mutated mCRPC**

**Niraparib/
Abiraterone**

EMA-Approved Indication⁶

In combination with prednisone/prednisolone for the treatment of adult patients with **BRCA-mutated (germline and/or somatic) mCRPC in whom chemotherapy is not clinically indicated**

FDA-Approved Indication⁷

In combination with enzalutamide for the treatment of adult patients with **HRR-mutated mCRPC**

Talazoparib

EMA-Approved Indication⁸

In combination with enzalutamide for the treatment of adult patients with **mCRPC in whom chemotherapy is not clinically indicated**

Select Phase III Trials of PARP Inhibitors in mHSPC

Trial	Patient Population	Treatment
AMPLITUDE (NCT04497844)	mHSPC (mCSPC) with HRRm	Niraparib + abiraterone/prednisone vs abiraterone/prednisone
TALAPRO-3 (NCT04821622)	mHSPC with DDR deficiency	Talazoparib + enzalutamide vs placebo + enzalutamide

AR, androgen receptor; CRPC, castration-resistant prostate cancer; ctDNA, circulating tumor DNA; DDR, DNA damage repair; EMA, European Medicines Agency; HRR, homologous recombination repair; HRRm, homologous recombination repair mutation; LHRH, luteinizing hormone-releasing hormone; mCRPC, metastatic castration-resistant prostate cancer; mCSPC, metastatic castration-sensitive prostate cancer; mHSPC, metastatic hormone-sensitive prostate cancer; NGS, next-generation sequencing; NHA, new hormonal agent.

References

- Schostak. Eur Urol Oncol. 2023;S2588.
- Olaparib US PI.
- Olaparib SmPC.
- Rucaparib US PI.
- Niraparib US PI.
- Niraparib SmPC.
- Talazoparib US PI.
- Talazoparib SmPC.