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PARP inhibitors for metastatic castration-resistant prostate cancer: Enhancing patient–practitioner conversations

Practice aid for metastatic castration-resistant prostate cancer

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PARP inhibitor indications in mCRPC

	1L			2L	3L
	Olaparib + abiraterone*[1,2]	Talazoparib + enzalutamide[3,4]	Niraparib–abiraterone fixed dose[5,6]	Olaparib Monotherapy*[1,2]	Rucaparib monotherapy[7]
FDA	***BRCA*** mutation[†‡]	**HRR** mutation	***BRCA*** mutation[†‡]	**HRR** mutation[‡§] Progressed on enzalutamide/ abiraterone	Deleterious ***BRCA*** mutation[†§] Prior androgen receptor-directed therapy and taxane-based chemotherapy
EMA	-	-	***BRCA1/2*** mutation[§]	***BRCA1/2*** mutation[§] Progressed following prior therapy that included new hormonal agent	**Not approved**
	Where chemotherapy not clinically indicated				

Side effects shared across PARP inhibitors in mCRPC[1–7]

Common non-haematological

- Nausea/vomiting
- Diarrhoea/constipation
- Asthenia/fatigue

Common haematological

- Anaemia
- Thrombocytopenia
- Neutropenia/lymphopenia

Rare, serious

- AML
- MDS
- Pneumonitis

Patients should be **monitored for haematological toxicity** and treatment discontinued if MDS/AML confirmed. Treatment should be interrupted if pneumonitis is suspected and discontinued if confirmed.

*Plus prednisone/prednisolone; [†]As determined by FDA-approved test; [‡]Deleterious or suspected deleterious mutation; [§]Germline/somatic.

Molecular testing for HRR alterations in prostate cancer

Guidelines recommend **germline and somatic** (tumour) HRR testing for **all patients with mCRPC**[8–10]

NCCN guidelines also recommend germline testing in patients with:[11]
Specified family history
Regional (node-positive) PC
High-risk localized PC
Very high-risk localized PC
Ashkenazi Jewish ancestry

≥1 close blood relative* with:
- Breast cancer at age ≤50 years
- Male breast cancer
- Ovarian cancer
- Pancreatic cancer
- Metastatic, node-positive, high- or very high-risk prostate cancer

≥3 close blood relatives* with:
- Any grade prostate cancer and/or breast cancer

Practical testing considerations

Germline testing samples[12]

- **Blood sample**
- **Saliva sample**

Somatic testing samples[8,9,12]

- **Metastatic tumour biopsy (ideal)**
- **Liquid biopsy (ctDNA)**
- **Primary tumour biopsy**
- **Primary prostatectomy tissue**

- Somatic sample test failures commonly occur due to sample degradation, insufficient tumour cellularity or limited sample availability[12]
- Caution is needed when interpreting ctDNA-only evaluation due to potential false-positive signal from CHIP[8]

Pre- and post-test genetic counselling are essential to inform patients about germline findings that may affect their familial cancer risk[11]

*Close blood relatives include first-, second-, and third-degree relatives on the same side of the family.

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Shared decision-making for PARP inhibitor use in mCRPC

EDUCATE

- Communicate big picture of treatment plan early
- Remind of next steps as they approach
- Share timely, up-to-date information with patients and caregivers
    - For example, specific information about therapy options, MoA and side effects

EMPHASIZE

- Communicate that PARP inhibitors work differently than traditional chemotherapy…
- …and have unique actions and side effects
- Encourage patients to report AEs early
- Assess and document AEs consistently at each clinic visit

EQUIP

- Provide patients with AE ‘toolkits’ specific to treatment plan phase:
    - Handout/wallet card to grade AEs
    - Supportive care medications including anti-diarrhoeal medications, stool softeners or anti-nausea medications
- Encourage early reporting, give patients permission to call

Abbreviations and references

Abbreviations

1L, first line; 2L, second line; 3L, third line; AE, adverse event; AML, acute myeloid leukaemia; BRCA, BReast CAncer gene; CHIP, clonal haematopoiesis of indeterminate potential; ctDNA, circulating tumour DNA; EMA, European Medicines Agency; FDA, US Food and Drug Administration; HRR, homologous recombination repair; mCRPC, metastatic castration-resistant prostate cancer; MDS, myelodysplastic syndrome; MoA, mechanism of action; PARP, poly (ADP-ribose) polymerase; PC, prostate cancer.

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