PRACTICE AID

Novel Approaches in Advanced Prostate Cancer[1-3]

PeerView Oncology

MLI Medical Learning Institute, Inc.

Selected Trials of PARP Inhibitor Monotherapy[1]

Phase 2

TRITON2 (NCT02952534)
Rucaparib
Active, not recruiting (N = 360)
FDA Approved May 15, 2020[2a]
- mCRPC; progression on AR-directed therapy; one prior taxane; HRR gene aberration
- No prior PARP inhibitor, mitoxantrone, cyclophosphamide, or platinum-based chemotherapy
- **Primary endpoints: ORR and PSA response**

LODESTAR (NCT04171700)
Rucaparib
Planned, N = 200
Recruiting
- mCRPC with HRR mutations excluding *BRCA1/2*
- At least one prior line of therapy
- ECOG PS 0-1
- **Primary endpoint: ORR**

TOPARP-B (NCT01682772)
Olaparib
Active, not recruiting (N = 98)
- mCRPC; ongoing ADT or prior bilateral orchiectomy
- Previously treated with one or two lines of taxane-based chemotherapy and/or AR-directed therapy
- **Primary endpoint: RR**

GALAHAD (NCT02854436)
Niraparib
Planned, N = 301
Recruiting
- mCRPC previously treated with ≥1 line of taxane-based chemotherapy; received ≥1 line of AR-targeted therapy
- DDR anomalies
- **Primary endpoint: ORR**

TALAPRO-1 (NCT03148795)
Talazoparib
Active, not recruiting (N = 100)
- mCRPC; metastatic disease in bone
- Assessment of DDR mutation status
- ECOG PS 0-2
- **Primary endpoint: ORR**

Phase 3

PROfound (NCT02987543)
Olaparib
Active, not recruiting (N = 387)
FDA Approved May 19, 2020[3b]
- mCRPC; ongoing ADT or prior bilateral orchiectomy
- Previously treated with AR-targeted therapy
- **Primary endpoint: rPFS**

TRITON3 (NCT02975934)
Rucaparib
Planned, N = 400
Recruiting
- mCRPC previously treated with one next-generation AR-targeted therapy
- Deleterious mutation in *BRCA1/2* or *ATM*
- **Primary endpoint: rPFS**

Access the activity, "Targeting DNA Repair Defects Through PARP Inhibition in Prostate Cancer: Rationale, Evidence, and Clinical Implications," at **PeerView.com/JEP40**

PRACTICE AID

Novel Approaches in Advanced Prostate Cancer[1-3]

PeerView Oncology

MLI Medical Learning Institute, Inc.

Combination Approaches With PARP Inhibitors

Selected Trials: Combinations With Novel Hormonal Agents

Recruiting

Phase 3 PROpel (NCT03732820)
Olaparib + abiraterone
Planned, N = 720

- mCRPC; ongoing ADT or prior bilateral orchiectomy
- ECOG PS 0-1
- Assessment of HRR gene aberrations
- **Primary endpoint: rPFS**

Recruiting

Phase 3 MAGNITUDE (NCT03748641)
Niraparib + abiraterone
Planned, N = 1,000

- mCRPC; ongoing ADT or prior bilateral orchiectomy
- **Primary endpoint: rPFS**

Recruiting

Phase 3 TALAPRO-2 (NCT03395197)
Talazoparib + enzalutamide
Planned, N = 1,037

- mCRPC; metastatic disease in bone
- Assessment of DDR mutation status
- ECOG PS 0-1
- **Primary endpoints: dose and rPFS**

Selected Trials: Combinations With PD-1/PD-L1 Inhibitors

Recruiting

Phase 2 CheckMate -9KD (NCT03338790)
Nivolumab + rucaparib or docetaxel or enzalutamide
Planned, N = 330

- mCRPC; ongoing ADT
- Plasma and fresh or archival tumor tissue
- ECOG PS 0-1
- HRD status
- **Primary endpoints: ORR and PSA response**

Phase 2 JAVELIN PARP MEDLEY (NCT03330405)
Avelumab + talazoparib
Planned, N = 242

- Locally advanced or mCRPC
- Primary or metastatic tumor biopsy
- ECOG PS 0-1
- **Primary endpoints: DLTs and OR**

Recruiting

Phase 3 KEYLYNK-010 (NCT03834519)
Pembrolizumab + olaparib
Planned, N = 780

- mCRPC
- Failed to respond to either abiraterone acetate or enzalutamide and to chemotherapy
- **Primary endpoints: rPFS and OS**

[a] On May 15, 2020, the FDA approved rucaparib for patients with deleterious germline/somatic *BRCA* mutation-associated mCRPC previously treated with AR-directed therapy and a taxane-based chemotherapy. [b] On May 19, 2020, the FDA approved olaparib for adult patients with deleterious/suspected deleterious germline/somatic HRR gene-mutated mCRPC following progression on enzalutamide of abiraterone.

ADT: androgen deprivation therapy; AR: androgen receptor; DDR: DNA damage repair; DLT: dose-limiting toxicity; ECOG PS: Eastern Cooperative Oncology Group Performance Status; HRD: homologous recombination deficiency; HRR: homologous recombination repair; mCRPC: metastatic castration-resistant prostate cancer; OR: overall response; ORR: objective response rate; PARP: poly (ADP-ribose) polymerase; PD-1: programmed cell death protein 1; PD-L1: programmed death ligand 1; PSA: prostate-specific antigen; rPFS: radiographic progression-free survival; RR: response rate.

1. https://clinicaltrials.gov. 2. https://www.fda.gov/drugs/fda-grants-accelerated-approval-rucaparib-brca-mutated-metastatic-castration-resistant-prostate. 3. https://www.fda.gov/drugs/drug-approvals-and-databases/fda-approves-olaparib-hrr-gene-mutated-metastatic-castration-resistant-prostate-cancer.

Access the activity, "Targeting DNA Repair Defects Through PARP Inhibition in Prostate Cancer: Rationale, Evidence, and Clinical Implications," at **PeerView.com/JEP40**