PARP Inhibitor–Based Combinations for the Management of Patients with Metastatic Castration-Resistant Prostate Cancer: What Are the Data Telling Us?
TOOLKIT

The Rationale for PARP Inhibitor–Based Combinations in mCRPC

Resource	Web Address
Abida W, Bryce AH, Vogelzang NJ, et al. 793PD Preliminary results from TRITON2: A phase II study of rucaparib in patients (pts) with metastatic castration-resistant prostate cancer (mCRPC) associated with homologous recombination repair (HRR) gene alterations. *Ann Oncol*. 2018:29(suppl 8):viii272. doi:10.1093/annonc/mdy284.002	https://www.annalsofoncology.org/article/S0923-7534(19)49323-X/fulltext
Abida W, Campbell D, Patnaik A, et al. 846PD Preliminary results from the TRITON2 study of rucaparib in patients(pts) with DNA damage repair (DDR)-deficient metastatic castration-resistant prostate cancer (mCRPC): Updated analyses. *Ann Oncol*. 2019;30(suppl 5):v327-v328. doi:10.1093/annonc/mdz248	https://www.annalsofoncology.org/article/S0923-7534(19)59062-7/fulltext
Abida W, Campbell D, Patnaik A, et al. Non-BRCA DNA damage repair gene alterations and response to the PARP inhibitor rucaparib in metastatic castration-resistant prostate cancer: Analysis from the phase II TRITON2 study. *Clin Cancer Res*. 2020;26(11):2487-2496. doi:10.1158/1078-0432.CCR-20-0394	https://pubmed.ncbi.nlm.nih.gov/32086346/
Abida W, Patnaik A, Campbell D, et al. Rucaparib in men with metastatic castration-resistant prostate cancer harboring a *BRCA1* or *BRCA2* Gene Alteration. *J Clin Oncol*. 2020;38(32):3763-3772. doi:10.1200/JCO.20.01035	https://pubmed.ncbi.nlm.nih.gov/32795228/
Armenia J, Wankowicz SAM, Liu D, et al. The long tail of oncogenic drivers in prostate cancer. *Nat Genet*. 2018;50(5):645-651. doi:10.1038/s41588-018-0078-z	https://pubmed.ncbi.nlm.nih.gov/29610475/
de Bono J, Mateo J, Fizazi K, et al. Olaparib for metastatic castration-resistant prostate cancer. *N Engl J Med*. 2020;382(22):2091-2102. doi:10.1056/NEJMoa1911440	https://pubmed.ncbi.nlm.nih.gov/32343890/

de Bono JS, Mehra N, Higano CS, et al. TALAPRO-1: Phase II study of talazoparib (TALA) in patients (pts) with DNA damage repair alterations (DDRm) and metastatic castration-resistant prostate cancer (mCRPC) – updated interim analysis (IA). *J Clin Oncol*. 2020;38(15 suppl):5566. doi:10.1200/JCO.2020.38.15_suppl.5566	https://ascopubs.org/doi/abs/10.1200/JCO.2020.38.15_suppl.5566
European Medicines Agency (EMA). Committee for Medicinal Products for Human Use (CHMP). Summary of opinion (post authorization). Lynparza (olaparib). September 17, 2020. Accessed May 16, 2022.	https://www.ema.europa.eu/en/documents/smop/chmp-post-authorisation-summary-positive-opinion-lynparza-ii-35-ii-36_en.pdf
Giri VN, Morgan TM, Morris DS, Berchuck JE, Hyatt C, Taplin ME. Genetic testing in prostate cancer management: Considerations informing primary care [published online ahead of print, 2022 Feb 24]. *CA Cancer J Clin*. 2022;10.3322/caac.21720. doi:10.3322/caac.21720	https://pubmed.ncbi.nlm.nih.gov/35201622/
Hussain M, Mateo J, Fizazi K, et al. Survival with olaparib in metastatic castration-resistant prostate cancer. *N Engl J Med*. 2020;383(24):2345-2357. doi:10.1056/NEJMoa2022485	https://pubmed.ncbi.nlm.nih.gov/32955174/
Johnson & Johnson. Janssen announces U.S. FDA breakthrough therapy designation granted for niraparib for the treatment of metastatic castration-resistant prostate cancer. October 3, 2019. Accessed May 16, 2022.	https://www.jnj.com/janssen-announces-u-s-fda-breakthrough-therapy-designation-granted-for-niraparib-for-the-treatment-of-metastatic-castration-resistant-prostate-cancer
Lynparza® (olaparib). Product characteristics. AstraZeneca AB; 2022. Accessed May 16, 2022.	https://www.ema.europa.eu/en/documents/product-information/lynparza-epar-product-information_en.pdf
Mateo J, Carriera S, Seed G, et al. Genomic profiling of primary prostate tumors from patients who develop metastatic castration-resistant prostate cancer (mCRPC). *J Clin Oncol*. 2018;36(15 suppl):5013. doi:10.1200/JCO.2018.36.15_suppl.5013	https://ascopubs.org/doi/10.1200/JCO.2018.36.15_suppl.5013
Mateo J, Seed G, Bertan C, et al. Genomics of lethal prostate cancer at diagnosis and castration resistance. *J Clin Invest*. 2020;130(4):1743-1751. doi:10.1172/JCI132031	https://pubmed.ncbi.nlm.nih.gov/31874108/
O'Connor MJ. Targeting the DNA damage response in cancer. *Mol Cell*. 2015;60(4):547-560. doi:10.1016/j.molcel.2015.10.040	https://pubmed.ncbi.nlm.nih.gov/26590714/
Pritchard CC, Mateo J, Walsh MF, et al. Inherited DNA-repair gene mutations in men with metastatic prostate cancer. *N Engl J Med*. 2016;375(5):443-453. doi:10.1056/NEJMoa1603144	https://pubmed.ncbi.nlm.nih.gov/27433846/

Robinson D, Van Allen EM, Wu YM, et al. Integrative clinical genomics of advanced prostate cancer. *Cell*. 2015;161(5):1215-1228. doi:10.1016/j.cell.2015.05.001	https://pubmed.ncbi.nlm.nih.gov/26000489/
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Talzenna® (talazoparib). Product characteristics. Pfizer Europe MA EEIG; 2021. Accessed May 16, 2022.	https://www.ema.europa.eu/en/documents/product-information/rubraca-epar-product-information_en.pdf
US Food and Drug Administration (FDA). FDA approves olaparib for gBRCAm metastatic pancreatic adenocarcinoma. December 27, 2019. Accessed May 16, 2022.	https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-olaparib-gbrcam-metastatic-pancreatic-adenocarcinoma
US Food and Drug Administration (FDA). FDA approves olaparib for HRR gene-mutated metastatic castration-resistant prostate cancer. May 19, 2020. Accessed May 16, 2022.	https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-olaparib-hrr-gene-mutated-metastatic-castration-resistant-prostate-cancer
US Food and Drug Administration (FDA). FDA grants accelerated approval to rucaparib for BRCA-mutated metastatic castration-resistant prostate cancer. May 15, 2020. Accessed May 16, 2022.	https://www.fda.gov/drugs/resources-information-approved-drugs/fda-grants-accelerated-approval-rucaparib-brca-mutated-metastatic-castration-resistant-prostate

Combination of PARP Inhibitors with Androgen-Signaling Inhibitors for mCRPC

Resource	Address
Chi KN, Rathkopf DE, Attard G, et al. A phase III randomized, placebo-controlled, double-blind study of niraparib plus abiraterone acetate and prednisone versus abiraterone acetate and prednisone in patients with metastatic prostate cancer (MAGNITUDE). *J Clin Oncol*. 2020;38(15 suppl):TPS5588. doi:10.1200/JCO.2020.38.15_suppl.TPS5588	https://ascopubs.org/doi/abs/10.1200/JCO.2020.38.15_suppl.TPS5588
ClinicalTrials.gov. NCT03395197. Talazoparib + Enzalutamide vs. Enzalutamide Monotherapy in mCRPC (TALAPRO-2). Last updated May 5, 2022. Accessed May 16, 2022.	https://clinicaltrials.gov/ct2/show/NCT03395197
ClinicalTrials.gov. NCT03732820 (PROpel). Study on Olaparib Plus Abiraterone as First-line Therapy in Men With Metastatic Castration-resistant Prostate Cancer. Last Updated April 5, 2022. Accessed May 16, 2022.	https://clinicaltrials.gov/ct2/show/NCT03732820

ClinicalTrials.gov. NCT03748641. A Study of Niraparib in Combination With Abiraterone Acetate and Prednisone Versus Abiraterone Acetate and Prednisone for Treatment of Participants With Metastatic Prostate Cancer (MAGNITUDE). Last updated April 22, 2022. Accessed May 16, 2022.	https://clinicaltrials.gov/ct2/show/NCT03748641
ClinicalTrials.gov. NCT04455750. A Clinical Study Evaluating The Benefit of Adding Rucaparib to Enzalutamide for Men With Metastatic Prostate Cancer That Has Become Resistant To Testosterone-Deprivation Therapy (CASPAR). Last updated April 19, 2022. Accessed May 16, 2022.	https://clinicaltrials.gov/ct2/show/NCT04455750
ClinicalTrials.gov. NCT04497844. A Study of Niraparib in Combination With Abiraterone Acetate and Prednisone Versus Abiraterone Acetate and Prednisone for the Treatment of Participants With Deleterious Germline or Somatic Homologous Recombination Repair (HRR) Gene-Mutated Metastatic Castration-Sensitive Prostate Cancer (mCSPC) (AMPLITUDE). Last updated April 27, 2022. Accessed May 16, 2022.	https://clinicaltrials.gov/ct2/show/NCT04497844
Kim N, Rathkopf DE, Smith MR, et al. Phase 3 MAGNITUDE study: First results of niraparib (NIRA) with abiraterone acetate and prednisone (AAP) as first-line therapy in patients (pts) with metastatic castration-resistant prostate cancer (mCRPC) with and without homologous recombination repair (HRR) gene alterations. *J Clin Oncol*. 2022;40(6 suppl):12. doi:10.1200/JCO.2022.40.6_suppl.012	https://ascopubs.org/doi/abs/10.1200/JCO.2022.40.6_suppl.012
Saad F, Armstrong AJ, Thiery-Vuillemin A, et al. PROpel: Phase III trial of olaparib (ola) and abiraterone (abi) versus placebo (pbo) and abi as first-line (1L) therapy for patients (pts) with metastatic castration-resistant prostate cancer (mCRPC). *J Clin Oncol*. 2022;40(6 suppl):11. doi:10.1200/JCO.2022.40.6_suppl.011	https://ascopubs.org/doi/abs/10.1200/JCO.2022.40.6_suppl.011

Personalization of Treatment for Patients with mCRPC with or without DDR Alterations

Resource	Address
American Cancer Society (ACS). Initial treatment of prostate cancer, by stage ans risk group. Last revised January 18, 2022. Accessed May 16, 2022.	https://www.cancer.org/cancer/prostate-cancer/treating/by-stage.html
Gleave ME, Bruchovsky N, Moore MJ, Venner P. Prostate cancer: 9. Treatment of advanced disease. *CMAJ*. 1999;160: 225-232. PMID:9951446	https://pubmed.ncbi.nlm.nih.gov/9951446/

Goodall J, Mateo J, Yuan W, et al. Circulating cell-free DNA to guide prostate cancer treatment with PARP inhibition. *Cancer Discov*. 2017;7(9):1006-1017. doi:10.1158/2159-8290.CD-17-0261	https://pubmed.ncbi.nlm.nih.gov/28450425/
National Comprehensive Cancer Network®. NCCN Clinical Practice Guidelines in Oncology. Prostate Cancer. Version 4.2022. May 10, 2022. Accessed May 16, 2022.	https://www.nccn.org/professionals/physician_gls/pdf/prostate.pdf
Parker C, Gillessen S, Heidenreich A, Horwich A; ESMO Guidelines Committee. Cancer of the prostate: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up *Ann Oncol*. 2015;26(suppl 5):v69-v77. doi:10.1093/annonc/mdv222	https://pubmed.ncbi.nlm.nih.gov/26205393/
Pongor LS, Munkácsy G, Vereczkey I, Pete I, Győrffy B. Currently favored sampling practices for tumor sequencing can produce optimal results in the clinical setting. *Sci Rep*. 2020;10(1):14403. doi:10.1038/s41598-020-71382-3	https://pubmed.ncbi.nlm.nih.gov/32873813/
Ryan JC. mCRPC Treatment: The right treatment for the right patient at the right time. URO Today. *Everyday Urology - Oncology Insights*. 2016;1(4). Accessed May 16, 2022.	https://www.urotoday.com/journal/everyday-urology-oncology-insights/articles/94104-mcrpc-treatment-the-right-treatment-for-the-right-patient-at-the-right-time-everyday-urology-full-text-article.html