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Efficacy and Safety of PARP Inhibitors in the Treatment of Prostate Cancer: An Umbrella Review of Systematic Reviews and Meta-Analyses

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ADMINISTRATIVE INFORMATION

Support - None.

Review Stage at time of this submission - Data extraction.

Conflicts of interest - None declared.

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 17 September 2024 and was last updated on 17 September 2024.

INTRODUCTION

Review question / Objective The objective of this umbrella review is to assess the safety and efficacy of PARP inhibitors (PARPi) in treating prostate cancer, focusing on specific patient subgroups defined by genetic alterations, such as BRCA1/2 mutations and homologous recombination deficiency (HRD).

Rationale Prostate cancer remains a significant health concern, particularly in advanced stages like metastatic castration-resistant prostate cancer (mCRPC). PARP inhibitors, initially developed to target DNA repair-deficient cancers, have shown promising results in treating mCRPC, particularly in patients with specific genetic mutations such as BRCA1/2. Given the growing body of research, a comprehensive umbrella review is required to synthesize the efficacy and safety of these therapies and optimize their use across diverse patient populations.

Condition being studied The PICO (Population, Intervention, Comparison, and Outcome) settings are as follows:

- P: Human participants diagnosed with prostate cancer, especially metastatic castration-resistant prostate cancer.
- I: Treatment with PARP inhibitors, including Olaparib, Rucaparib, Niraparib, Veliparib, and Talazoparib.
- C: Non-PARP inhibitor therapies, including standard hormonal therapies or other treatments.
- O: Overall survival (OS), progression-free survival (PFS), and adverse events (all-grade and high-grade).

METHODS

Search strategy Two authors will conduct independent electronic searches in PubMed, Embase, Cochrane CENTRAL, and ClinicalTrials.gov databases using the following search terms: ((poly(adp-ribose) polymerase inhibitors) OR (PARP Inhibitors) OR (PARP inhibitor)

OR ("PARP inhibitor*") OR ("Poly adp-ribose") OR (Olaparib) OR (Rucaparib) OR (Niraparib) OR (Veliparib) OR (Talazoparib) OR (Pamiparib) OR (Fluzoparib)) AND ("review" OR "systematic review" OR "meta-analysis") AND ('prostate cancer' OR prostate carcinoma OR prostate neoplasm).

Participant or population Human participants diagnosed with prostate cancer.

Intervention PARP inhibitors (e.g., Olaparib, Rucaparib, Niraparib, Veliparib, Talazoparib) with or without any combination therapy.

Comparator Any types.

Study designs to be included Systematic reviews and meta-analyses of randomized controlled trials (RCTs).

Eligibility criteria • Inclusion: Studies must report on systematic reviews and meta-analyses that assess at least one outcome about efficacy or safety of PARP inhibitors in treating prostate cancer.
• Exclusion: Narrative reviews, scoping reviews, abstracts, or studies without sufficient data on efficacy or safety of PARP inhibitors will be excluded.

Information sources Databases to be searched include PubMed, Embase, Cochrane CENTRAL, and ClinicalTrials.gov using the search strategy detailed above.

Main outcome(s) • Primary Outcomes: Overall survival (OS), progression-free survival (PFS), Adverse events (overall all-grade and high-grade).
• Secondary Outcomes: PSA response, overall response rate (ORR), Adverse events (by symptoms).

Data management Two independent reviewers will extract data, including effect sizes, research design, patient characteristics, and treatment details. The data will be carefully checked for consistency, and any discrepancies will be resolved through discussion.

Quality assessment / Risk of bias analysis The AMSTAR2 tool will be used to assess the methodological quality of the included systematic reviews and meta-analyses, focusing on key domains such as protocol registration, literature search comprehensiveness, and risk of bias.

Strategy of data synthesis The synthesis process involved sorting data by outcome types—overall survival (OS), progression-free survival (PFS), and adverse events—and organizing them based on treatment comparisons and symptoms for adverse events. If multiple similar data is presented, we adopted a systematic approach to select the most representative data for each study.

Subgroup analysis Genetic Alterations: BRCA1/2 mutations, Homologous recombination deficiency (HRD), ATM mutations etc. 2. PARP Inhibitor Variants: Olaparib, Rucaparib, Niraparib, Veliparib, Talazoparib.

Sensitivity analysis If sufficient data is available, a sensitivity analysis will be conducted to exclude the low-quality studies.

Language restriction No language restrictions will be applied.

Country(ies) involved Taiwan.

Keywords PARP inhibitors, prostate cancer, metastatic castration-resistant prostate cancer, BRCA1/2, homologous recombination deficiency.

Contributions of each author
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