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Comparative efficacy of olaparib in combination with or without novel antiandrogens for treating metastatic castration-resistant prostate cancer: A systematic review and network meta-analysis

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Corresponding author:
Xiaoqiang Liu

xiaoqiangliu1@163.com

Author Affiliation:
Tianjin Medical University General Hospital.

Chen, XY[1]; Pan, Y[2]; Wang, QH[3]; Ren, CZ[4]; Li, MW[5]; Hao, XX[6]; Xie, LJ[7]; Liu, XQ[8].

ADMINISTRATIVE INFORMATION

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Review Stage at time of this submission - The review has not yet started.

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 21 October 2023 and was last updated on 21 October 2023.

INTRODUCTION

Review question / Objective Population: only metastatic castration-resistant prostate cancer patients. Intervention: olaparib, olaparib plus abiraterone and apalutamide plus abiraterone. Comparison: abiraterone or enzalutamide. Outcome: radiologic progression-free survival, overall survival, time to second progression-free survival, circulating tumor cell conversion and adverse events. Study design: high-quality randomized controlled studies.

Condition being studied Prostate cancer is the second most common cancer after lung cancer and accounts for 7% of all new cancer diagnoses in men worldwide. The standard of care for metastatic castration-resistant prostate cancer (mCRPC) includes taxane-based chemotherapy, radiotherapy, and novel antiandrogens (NAA), such as abiraterone, enzalutamide, darolutamide, or apalutamide. Although these treatment options have shown the ability to improve overall survival (OS), subsequent NAA therapy is known to work only in a minority of patients and the responses are short-lived. There is an urgent need to evaluate non-NAA monotherapy approaches in light of the growing number of patients receiving their first NAA therapy before developing castration-resistant disease.

METHODS

Participant or population Eligible patients were adult (defined according to local regulation) males with pathologically confirmed prostate adenocarcinoma, without neuroendocrine differentiation, signet-cell, or small-cell features, and an Eastern Cooperative Oncology Group performance status score of 0 or 1. Eligible patients had metastatic disease, either de novo or after recurrence after prior local therapy,

documented by a positive bone scan, or metastatic lesions on computed tomography or magnetic resonance imaging. Enrollment was based on investigator-assessed metastases; after study entry, metastasis was evaluated by independent central review. Prior ADT and up to six cycles of prior docetaxel chemotherapy were permitted.

Intervention Patients took olaparib, olaparib plus abiraterone and apalutamide plus abiraterone.

Comparator Patients took placebo plus enzalutamide or abiraterone.

Study designs to be included Randomized controlled trials (RCTs) will be included.

Eligibility criteria The inclusion criteria for eligible studies were as follows: (a) randomized controlled design; (b) inclusion of only mCRPC patients; (c) provision of at least one of the following oncologic outcomes: radiologic progression-free survival (rPFS) or OS; (d) inclusion of primary and secondary endpoints; and (e) extraction of either the hazard ratio (HR) or the number of events from the text. The exclusion criteria were as follows: (a) publications that were duplicated or contained poor-quality information; (b) studies that contained insufficient primary data or incomplete study data; and (c) publications that were reviews, commentaries, letters, or case reports.

Information sources All data were obtained from PubMed, EMBASE, Cochrane Library, or ASCO University Meeting abstracts.

Main outcome(s) For each study, HR, the calculated odds ratio (OR) and confidence intervals (CI) were extracted for the reported primary and secondary endpoints, which included rPFS, OS, time to second progression-free survival (PFS2; defined as time from randomization to the investigator-assessed progression event [using Response Evaluation Criteria In Solid Tumors (RECIST) version 1.1 or Prostate Cancer Clinical Trials Working Group 2 (PCWG2) criteria] following that used for the primary rPFS analysis, or death), objective response rate (ORR; RECIST v 1.1, PCWG2) (Eisenhauer et al., 2009), PSA response (reduction of ≥50% from baseline, confirmed at the next assessment ≥4 weeks later), circulating tumor cell (CTC) conversion (change from ≥5 cells/7.5 mL at baseline to <5 cells/7.5 mL post-baseline). We also extracted the number of overall adverse events (AEs) and noted the number of severe adverse events (grade ≥3).

Quality assessment / Risk of bias analysis First, two researchers independently screened the literature and extracted data according to established criteria. The reasons for excluding the articles were also recorded. When a disagreement arose, both parties negotiated with or consulted a third-party expert. The quality of the included trials was assessed using the Cochrane Collaboration tool to assess the risk of bias in the randomized controlled trials.

Strategy of data synthesis The data were processed using Stata 16.0 and R 4.4.2. A Bayesian network meta-analysis was used for indirect comparisons of selected endpoints using the GeMTC package in R. We used the reported HR or calculated OR in the analysis. Considering that there was only one point of data for each intervention, no source of inconsistency was assessed; therefore, indirect comparisons between different interventions were obtained using a fixed-effects model. We used the rank probabilities for the primary and secondary endpoints to assess the preferred probability ranking for each drug.

Subgroup analysis Our study did not involve performing subgroup analyses.

Sensitivity analysis Given that there was only 1 point of data for each intervention, there was no source for assessment of inconsistency.

Country(ies) involved China.

Keywords Metastatic castration-resistant prostate cancer; Novel antiandrogens; The poly(ADP-ribose) polymerase inhibitor; Olaparib.

Contributions of each author

Author 1 - Xiangyu Chen.
Email: 13984417174@163.com
Author 2 - Yang Pan.
Email: panyang361@163.com
Author 3 - Qihua Wang.
Author 4 - Congzhe Ren.
Author 5 - Muwei Li.
Author 6 - Xuexue Hao.
Author 7 - Lijun Xie.
Author 8 - Xiaoqiang Liu.