INPLASY PROTOCOL

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None declared.

Efficacy and safety of PARP inhibitors in breast cancer: a systematic review and meta-analysis

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Review question / Objective: **Breast cancer is a serious threat to women's health. The aim of this study was to evaluate the efficacy and safety of poly (ADP-ribose) polymerase (PARP) inhibitors (PARPi) in patients with breast cancer.**
Condition being studied: **n recent years, BRCA as a molecular target has received increasing attention, and the advent of the era of poly (ADP-ribose) polymerase (PARP) inhibitors (PARPi) has provided a new targeted therapeutic regimen for patients with breast cancer.**
Eligibility criteria: **(i) pathologically diagnosed breast cancer; (ii) study phaseII/III; (iii) the experimental group consisted of PARPi monotherapy or PARPi in combination with chemotherapy, and chemotherapy combined with or without placebo was administered to the control group; (iv) the endpoints were progression-free survival (PFS), overall survival (OS), overall response rate (ORR) or adverse events (AEs); (v) included studies can directly extract or calculate hazard ratio (HR), risk ratio (RR) and 95% confidence interval (CI).**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 26 October 2022 and was last updated on 26 October 2022 (registration number INPLASY2022100105).

INTRODUCTION

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METHODS

Participant or population: Patients with breast cancer.

Intervention: The experimental group consisted of PARPi monotherapy or PARPi in combination with chemotherapy.

Comparator: Chemotherapy combined with or without placebo was administered to the control group.

Study designs to be included: (i) pathologically diagnosed breast cancer; (ii) study phaseII/III; (iii) the experimental group consisted of PARPi monotherapy or PARPi in combination with chemotherapy, and chemotherapy combined with or without placebo was administered to the control group; (iv) the endpoints were progression-free survival (PFS), overall survival (OS), overall response rate (ORR) or adverse events (AEs); (v) included studies can directly extract or calculate hazard ratio (HR), risk ratio (RR) and 95% confidence interval (CI).

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Information sources: PubMed, EMBASE, Cochrane Library, and Web of Science.

Main outcome(s): Eight RCTs were included in the study. Compared with the chemotherapy group, PARPi group significantly improved PFS (HR=0.68, 95%CI 0.61-0.76, P<0.00001), OS (HR=0.84, 95%CI 0.73-0.95, P=0.006) and ORR (RR=1.46, 95%CI 1.10-1.93, P=0.008) in patients with breast cancer. Subgroup analyses based on the type of intervention, BRCA mutation status, hormone receptor status, previous platinum and cytotoxic therapy, and the history of central nervous system metastases showed that the PARPi group significantly prolonged PFS. In terms of safety, the PARPi group increased the incidence of grade≥3 thrombocytopenia and the difference was statistically significant (RR=1.34, 95%CI 1.13-1.59, P=0.0007).

Quality assessment / Risk of bias analysis: The criteria used to assess the quality of the literature were as follows: (i) random sequence; (ii) allocation concealment; (iii) blinding of participants and personnel; (iv) blinding of outcomes; (v) incomplete outcome data; (vi) selective reporting, and (vii) other biases: “low risk,” “high risk,” and “unclear” were made for each item.

Strategy of data synthesis: This study was carried out using the Review Manager 5.3 software. PFS and OS were analyzed using the HR and 95%CI, and the subgroup analyses were performed by the type of intervention and the baseline characteristics of patients. ORR and AEs were analysed using RR and 95%CI. P value <0.05 was considered statistically significant. We judged heterogeneity according to the Cochran’s Q and I^2values. Cochran Q P0.1 and I^2<50% was used. To assess the reliability of the results, the symmetry of the funnel plots was used to assess the publication bias.

Subgroup analysis: the subgroup analyses were performed by the type of intervention and the baseline characteristics of patients.

Sensitivity analysis: We judged heterogeneity according to the Cochran’s Q and I^2values. Cochran Q P<0.1 or I^2≥50% indicated heterogeneity among the included studies, using the random effect model and sensitivity analysis if necessary.

Country(ies) involved: China.

Keywords: breast cancer, PARP inhibitors, chemotherapy, meta-analysis.

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