INPLASY PROTOCOL

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Corresponding author:
Kexiang Zhu

flexzhu69102020@163.com

Author Affiliation:
The First Hospital of Lanzhou University

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Conflicts of interest:
There is no conflicts of interest.

The efficacy and adverse effects of PARP inhibitor combined with chemotherapy compared with chemotherapy alone in the treatment of cancer patient：A protocol for systematic review

Zhao, SY[1]; Tao, F[2]; Yao, L[3], Zheng, Y[4]; Zhang, L[5]; Zhu, KX[6]

Review question / Objective: **Study type: We included phase 2 and phase 3 clinical trials comparing PARP inhibitor combined with chemotherapy and chemotherapy alone. There are no language restrictions on the study. Non-RCT research will be excluded. Research objects: All cancer patients were included in this study, without restrictions on country, gender, age, race, and tumor type. Intervention measures: Cancer patients were included in clinical trials. The experimental group was PARP inhibitor combined with chemotherapy and the control group was chemotherapy alone. Regardless of whether the treatment is first-line treatment, regardless of the order of administration and dosage changes, regardless of whether the patient is an advanced cancer patient. Exclude patients who use other similar drugs at the same time or in combination with other chemotherapy drugs. Outcome: Outcome indicators include overall survival (OS), progression-free survival (PFS), objective response rate (ORR) and adverse effects. The adverse effects include: abdominal pain, constipation, diarrhea, fatigue, nausea, vomiting, loss of appetite, anemia, neutropenia, and thrombocytopenia.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 24 September 2020 and was last updated on 24 September 2020 (registration number INPLASY202090087).

INTRODUCTION

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Condition being studied: In the world, tumors are one of the most important diseases that increase the burden of human economy and medical care. Although with the development of medical treatment, the survival time of patients can be prolonged through various treatments such as surgery and drugs, there is no doubt that tumors are still an unsolved problem. In the past ten years, the research of PARP inhibitors has made great breakthroughs and progress. Become a new type of medicine for cancer treatment, bringing hope to more advanced cancer patients. PARP inhibitor monotherapy has achieved great success, but PARP combination therapy is unknown. PARP inhibitors in combination with chemotherapy, antiangiogenic agents, and immunotherapy have a positive or negative effect on treatment.Which type of combination can give patients the greatest benefit and the least side effects is still a question we need to explore.

METHODS

Participant or population: All cancer patients were included in this study, without restrictions on country, gender, age, race, and tumor type.

Intervention: The experimental group was PARP inhibitor combined with chemotherapy.

Comparator: control group was chemotherapy alone.

Study designs to be included: We included phase 2 and phase 3 clinical trials comparing PARP inhibitor combined with chemotherapy and chemotherapy alone.

Eligibility criteria: All cancer patients were included in this study, without restrictions on country, gender, age, race, and tumor type.

Information sources: We searched the following four databases, including: PubMed, EMBASE, Web of Science and Cochrane Library. The search will also be conducted at the clinical trial centers: ClinicalTrials.gov, ISRCTN Registry, WHO International Clinical Trials Registration Platform. If you find any data that cannot be extracted in the literature, contact the corresponding author of the article by email.

Main outcome(s): Outcome indicators include overall survival (OS), progression-free survival (PFS).

Quality assessment / Risk of bias analysis: We use the Cochrane Intervention Systematic Review Manual, and will follow the guidance in the latest edition of the Cochrane Manual to systematically review the included literature. This process was completed by two researchers individually, and a third party resolved any disagreements. The researchers evaluated the risks according to the following criteria, and the risks were divided into three levels: "high", "low" or "unclear".

Strategy of data synthesis: A meta-analysis of the data was performed after the data in the included literature was extracted. RevMan 5.3 version was used for data analysis. Binary variables are represented by OR and 95% CI, and time-event data are represented by HR and 95% CI. Use the inverse variance method to calculate the

combined HR. Since this study included different types of tumors, random effects models were used to reduce heterogeneity and increase reliability.

Subgroup analysis: We use subgroup analysis to analyze the causes of heterogeneity. It is possible to perform subgroup analysis for different tumor types, ages, genders, races, and no chemotherapy regimens.

Sensibility analysis: Perform sensitivity analysis to resolve the impact of each study on synthesis. We also evaluate the impact of sample size and missing data on the results. The funnel chart is used to assess the risk of publication bias. Using Begg's and Egger's tests to assess publication bias, $p < 0.05$ was considered statistically significant.

Country(ies) involved: China.

Keywords: PARP inhibitors, chemotherapy, Neoplasms, protocols, randomized controlled trials, systematic reviews.

Contributions of each author:
Author 1 - Suyue Zhao designed a systematic review and provided research ideas.
Author 2 - Tao Fang designed a systematic review and provided research ideas.
Author 3 - Li Yao revised the manuscript.
Author 4 - Ying Zheng revised the manuscript, independently screened articles, extracted data, assessed bias and processed data.
Author 5 - Ling Zhang independently screened articles, extracted data, assessed bias and processed data.
Author 6 - Kexiang Zhu any objections will be arbitrated by Zhu Kexiang.