INPLASY PROTOCOL

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Conflicts of interest:
None declared.

Efficacy and safety of selinexor in the treatment of AML
A protocol for systematic review and meta-analysis

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Review question / Objective: **Acute myeloid leukemia (AML) is the most common leukemia among the adult population and accounts for about 80% of all cases. Despite advancements in therapeutic regimens, the prognosis remains very poor, especially in the elderly population. Selinexor is a first-in-class, oral, small molecule Exportin-1 (XPO1) inhibitor that is being developed for the treatment of a variety of cancers, including AML. The efficacy and safety issues of selinexor in the treatment of AML are still the focus of attention. Therefore, we conducted a meta analysis to evaluate the efficacy and safety of selinexor in the treatment of AML.**
Condition being studied: **Acute myeloid leukemia. According to the search strategy, regardless of publication date or language, randomized controlled trials (RCTs) of Selinexor for AML will be retrieved from 8 databases. First of all, the literature was screened according to the eligibility criteria, and use the Cochrane Collaboration's tool to assess the quality of the included literature. Then, using Rev Man 5.3 and STATA 14.2 software for traditional meta-analysis. Finally, the evaluation of the quality of the evidence and the strength of the recommendations will adopt the Grading of Recommendations, Assessment, Development and Evaluation method.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 17 October 2021 and was last updated on 17 October 2021 (registration number INPLASY2021100056).

INTRODUCTION

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METHODS

Participant or population: Patients with AML diagnosed by WHO criteria diagnosis of AML will be included. There are no restrictions on nationality, age, sex, or race. Patients with severe liver and kidney, or other uncontrolled systemic diseases are excluded.

Intervention: The recommended phase II dose (RP2D) of selinexor was 60 mg twice weekly in the treatment group.

Comparator: The control group was only given routine chemotherapy , or the same dose of placebo was given on the basis of routine chemotherapy. Routine chemotherapy regimens mainly include cytarabine plus idarubicin(IA), high dose cytarabine and mitoxantrone(MA), decitabine, cytarabine, etoposide and Mitoxantrone (MAE) , cytarabine, cladribine and granulocyte-colony stimulating factor (CLAG), cytarabine and fudarabine(FA)

Study designs to be included: Randomized controlled trials (RCTs) will be included in this study irrespective of language or publication category. Animal trials, review article and studies with incorrect RCT designs will be excluded.

Eligibility criteria: We will formulate the inclusion and exclusion criteria for this study based on the PICOS principles.

Information sources: Use endnoteX9.0 software to manage literature. After searching literature based on the above steps, import them into endnote software for literature screening. First, 2 independent researchers will conduct a preliminary literature screening based on the titles and abstracts of the included literature to eliminate duplicate and non-RCTs. Then read the full text of the remaining literature according to the previously designed principles of eligibility criteria, and finally determine the appropriate literature.

Main outcome(s): The primary outcomes include ORR,CR,CRi and DOR.

Additional outcome(s): The secondary outcomes include decrease in bone marrow blasts from baseline, quality of life (QOL), etc; the safety indicators include thrombocytopenia, fatigue, nausea, anaemia, decreased appetite, decreased weight, diarrhoea, vomiting, hyponatremia, neutropenia, leukopenia, constipation, and other adverse events(AEs).

Quality assessment / Risk of bias analysis: Two reviewers will independently assess the quality of the included literature according to the Cochrane Collaboration's tool for RCTs. If there is a disagreement between 2 reviewers, the third reviewer resolves the issue. According to Cochrane Handbook V.5.2.0, characteristics of each item will be evaluated in 3 categories: low, unclear, and high[13]. The results of the quality assessment will be completed using software Review Manager 5.3.

Strategy of data synthesis: Retrieve the databases by combining subject words

with random words. Appropriate adjustments will be made according to the grammatical rules of different databases to ensure the completeness and comprehensiveness of the search. We will firstly conduct a pre- search, and discuss the problems encountered in the search process with the team. After confirming that there are no problems, we will conduct a formal literature search.

Subgroup analysis: Taking into account the issue of heterogeneity, we will conduct a subgroup analysis based on the specifific circumstances of the included literature. If there is a problem of heterogeneity, we will conduct.

Sensitivity analysis: This systematic review will use the method of eliminating each study one by one for sensitivity analysis. If the effective indicators of selinexor in the treatment of AML have not changed significantly, it indicates that the study is robustness. On the contrary, it is not robustness. According to the specific situation, low-quality research is excluded.

Country(ies) involved: China.

Other relevant information: There are no restrictions on nationality, age, sex, or race.

Keywords: Acute myeloid leukemia, Selinexor, meta-analysis, systematic review.

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