## INPLASY PROTOCOL

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# Comparison of therapeutic effects of various stem cell types, sources, and routes of administration on chronic decompensated cirrhosis: protocol for a network meta-analysis

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Review question / Objective: The aim of this study was to compare the therapeutic effects of various stem cell types. sources and routes of administration on chronic decompensated cirrhosis by using network meta-analysis. Condition being studied: Liver cirrhosis is an important public health problem that puzzles the world. It is divided into compensatory stage and decompensated stage. Once the patient enters decompensated stage, the treatment is very limited, and liver transplantation is currently the best and only approach to improve the survival rate of decompensated cirrhosis4. However, liver transplantation is difficult to be widely applied due to the lack of donor organs and high cost. Therefore, it is very important to study the alternative treatment of liver transplantation. Stem cell therapy as a promising frontier treatment for decompensated cirrhosis, is becoming one of the best feasible alternatives to liver transplantation in recent 20 years. It is very important and necessary to optimize the factors such as cell sources, types, and delivery route, etc. before taking stem cell therapy as a routine clinical treatment. It is believed that the network metaanalysis of the efficacy of various types of stem cells from different sources and routes of administration in the treatment of chronic decompensated cirrhosis can provide useful very clues for clinical practice.

**INPLASY registration number:** This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 17 January 2023 and was last updated on 12 March 2023 (registration number INPLASY202310050).

#### INTRODUCTION

Review question / Objective: The aim of this study was to compare the therapeutic

effects of various stem cell types, sources and routes of administration on chronic decompensated cirrhosis by using network meta-analysis.

Condition being studied: Liver cirrhosis is an important public health problem that puzzles the world. It is divided into compensatory stage and decompensated stage. Once the patient enters decompensated stage, the treatment is very limited, and liver transplantation is currently the best and only approach to improve the survival rate of decompensated cirrhosis4. However, liver transplantation is difficult to be widely applied due to the lack of donor organs and high cost. Therefore, it is very important to study the alternative treatment of liver transplantation. Stem cell therapy as a promising frontier treatment for decompensated cirrhosis, is becoming one of the best feasible alternatives to liver transplantation in recent 20 years. It is very important and necessary to optimize the factors such as cell sources, types, and delivery route, etc. before taking stem cell therapy as a routine clinical treatment. It is believed that the network meta-analysis of the efficacy of various types of stem cells from different sources and routes of administration in the treatment of chronic decompensated cirrhosis can provide useful very clues for clinical practice.

### **METHODS**

Participant or population: All individuals must be at least 18 years old and have had a decompensated liver cirrhosis diagnosis. Gender, race, nationality and language are not factors in eligibility.

Intervention: Various types of stem cells of different sources and routes of administration.

Comparator: Placebo, matched medical treatment, or another stem cells of different source, type or route of administration.

Study designs to be included: Randomized controlled trials only.

Eligibility criteria: The following were the criteria for inclusion: (1) Study subjects: patients who have been diagnosed with chronic decompensated cirrhosis; (2)

Interventions: at least one of the intervention arms include stem cells of various types, sources, and delivery routes; (3) Control group: patients received matched medical therapy, placebo, or stem cells of different types, sources or delivery routes; (4) Study design: randomized controlled trial (RCT); (5) Outcome index: the research reported the model of end-stage liver disease (MELD) score; (6) There are no language restrictions; (7) Patients are at least 18years old.

Information sources: PubMed, Embase, Cochrane library, Web of science, clinicaltrials.gov

Main outcome(s): The model of end-stage liver stage (MELD) score is the main outcome of measurement.

Additional outcome(s): Survival rate will be the secondary outcome of interest.

Quality assessment / Risk of bias analysis: Using the Revised Cochrane risk-of-bias tool for randomized controlled trials (RoB2), the risk of bias for each included study will be evaluated.

Strategy of data synthesis: We utilized Stata software (version 15.1) to create the data network map, which displayed the direct and indirect comparisons between the included studies and the various interventions.

The consistency test was performed to determine the presence of heterogeneity. If P<0.05, inconsistency was indicated. We used the rank likelihood raking chart to rank diver stem cells of various sources, types and delivery routes. Finally, funnel plots were utilized to determine whether a selection bias exists. Using Egger's test and Begg's test, the potential influence of publication bias on the study's findings was also examined.

Subgroup analysis: No subgroup analysis in the study.

Sensitivity analysis: No sensitivity analysis in the study.

Language restriction: No language restrictions in the study.

Country(ies) involved: PR China, the United Kingdom of Great Britain and Northern Ireland.

Keywords: Stem cells, efficacy, comparison, decompensated liver cirrhosis, network meta-analysis.

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