INPLASY PROTOCOL

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Conflicts of interest:
None declared.

Efficacy and safety of tandem versus single autologous hematopoietic stem cell transplantation for the treatment of multiple myeloma: A protocol for systematic review and meta-analysis

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Review question / Objective: **Multiple myeloma (MM) is a B-lymphocytic lymphoma originated from malignant plasma cells in bone marrow. Although autologous hematopoietic stem cell transplantation (AHSCT) can improve the progression-free survival (PFS) of most MM patients, recurrence is inevitable. Some patients (such as some high-risk cytogenetics patients) have limited improvement in PFS through a single AHSCT. It has been reported that tandem and single AHSCT can improve the clinical efficacy of some MM patients, but it is not clear which part of patients can benefit from PFS or overall survival (OS). Therefore, the present study aimed to comprehensively evaluate the efficacy and safety of tandem and single AHSCT in the treatment of MM through systematic review and meta-analysis.**
Condition being studied: **In this study, evidence-based medicine will be used to comprehensively search the scientific and technological literature database to obtain relevant research literature, and the quality of literature will be screened and evaluated according to the established standards. The total sample size will be expanded by combining with other relevant randomized controlled trials to minimize bias in the study.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 29 June 2021 and was last updated on 29 June 2021 (registration number INPLASY202160112).

INTRODUCTION

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progression-free survival (PFS) of most MM patients, recurrence is inevitable. Some patients (such as some high-risk cytogenetics patients) have limited improvement in PFS through a single AHSCT. It has been reported that tandem and single AHSCT can improve the clinical efficacy of some MM patients, but it is not clear which part of patients can benefit from PFS or overall survival (OS). Therefore, the present study aimed to comprehensively evaluate the efficacy and safety of tandem and single AHSCT in the treatment of MM through systematic review and meta-analysis.

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METHODS

Search strategy: We will conduct several pre-searches, carefully discuss the matters needing attention in literature retrieval, and finally formulate the retrieval strategy. The search databases are as follows: PubMed, Cochrane Library, CNKI, Cochrane Controlled Trial Center Registration, VIP Database, EMBASE, Wanfang Database, ScienceNet. The search strategy consists of grid and keywords.

Participant or population: (1) It is consistent with the clinical diagnostic criteria of MM8 (2) The diagnosis of each study group is clear, all of them are primary patients. (3) The data included in the research is reliable and the sample size was clear. (4) Select one of the duplicate documents or reports on the same population. (5) There are no restrictions on race, nationality, gender, age, or region. (6) Patients with other complex and serious diseases are not included. No previous history of coagulopathy and other tumor diseases.

Intervention: The intervention group was treated with tandem autologous hematopoietic cell transplantation, and the control group was treated with single autologous hematopoietic cell transplantation. In the actual treatment, in order to ensure the normal vital signs of patients, the control group and the intervention group need to take the drugs to protect organs and provide nutrition according to the conventional treatment, and at the same time, the blood examination should be carried out regularly. The number of blood tests was more than or equal to twice a week, and the patients were observed to take drugs according to the clinical symptoms.

Comparator: The control group was treated with single autologous hematopoietic cell transplantation.

Study designs to be included: The study will contain all relevant randomized controlled trials (RCT) and systematic review/meta-analysis of different doses of tandem versus single autologous hematopoietic cell transplantation for the treatment of multiple myeloma（MM). Case reports, overview, non-RCT, or semi-RCT trials, will not be included in the study, and the language will be confined to Chinese or English.

Eligibility criteria: (1) The identification of MM does not meet the criteria of this article; (2) The patients with MM who have been diagnosed and treated or experienced radiotherapy and chemotherapy, secondary MM; (3) Lack of literature on main research indicators; (4) A history of other malignant tumors in the past 3 years; (5) Literature review without control study; (6) Literature with incomplete or false clinical data; (7) No support for follow-up treatment.

Information sources: Use endnoteX9.0 software to manage literature, and all duplicate references will be deleted. First, two independent researchers will conduct a preliminary literature screening. When the two researchers disagreed, the controversial literatures were discussed to

decide whether they should be included. If necessary, a third-party researcher can help solve the problem and explain why. If any information in the attached literature is incomplete, we will contact the author by email to obtain the corresponding data.

Main outcome(s): Overall survival (OS) and progression-free survival (PFS).

Additional outcome(s): Including stringent complete response (sCR), complete remission (CR), very good partial response (VGPR), partial response (PR), minimal response (MR), stable disease (SD), progressive disease (PD), clinical recurrence, recurrence after CR.

Quality assessment / Risk of bias analysis: Two independent reviewers will evaluate the quality of the included articles based on the Cochrane Collaboration randomized controlled trial tool. According to Cochrane manual v.5.2.0, the characteristics of each project will be divided into three 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: We will conduct several pre-searches, carefully discuss the matters needing attention in literature retrieval, and finally formulate the retrieval strategy. The search databases are as follows: PubMed, Cochrane Library, CNKI, Cochrane Controlled Trial Center Registration, VIP Database, EMBASE, Wanfang Database, ScienceNet. The search strategy consists of grid and keywords.

Subgroup analysis: Taking into account the issue of heterogeneity, we will conduct a subgroup analysis of the reasons for the heterogeneity according to the source of the heterogeneity. If there is a problem of heterogeneity, we will use several aspects such as gender, age, treatment type, disease course, country, publication year, onset time, and duration for group analysis in different design schemes.

Sensitivity analysis: This systematic review will use the exclusion method to analyze the sensitivity of all outcome indicators to disease. If the heterogeneity changes after changing some important factors that may affect the results, it is the cause of heterogeneity. On the contrary, if the quality does not change, the sensitivity is low and the result is stable and reliable.

Country(ies) involved: China.

Keywords: MM, AHSCT, tandem AHSCT, protocol, systematic review.

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