International Platform of Registered Systematic Review and Meta-analysis Protocols

INPLASY

Addition of daratumumab to Standard Triple-drug Regimens Achieved Better Efficacy but Higher Toxicities in Newly Diagnosed Multiple Myeloma: A Systematic Review and Meta-analysis of randomized controlled trials

INPLASY2024120026
doi: 10.37766/inplasy2024.12.0026
Received: 7 December 2024
Published: 7 December 2024

Hu, B; Fang, D; Cao, J; Li, TQ; Wang, W.

Corresponding author:
Jun Wang

angela80824w@sina.com

Author Affiliation:
Changde Hospital, Xiangya School of Medicine, Central South University.

ADMINISTRATIVE INFORMATION

Support - No supporting.

Review Stage at time of this submission - Data analysis.

Conflicts of interest - None declared.

INPLASY registration number: INPLASY2024120026

Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 7 December 2024 and was last updated on 7 December 2024.

INTRODUCTION

Review question / Objective The recommendations regarding the adoption of triple-drug regimens versus daratumumab-incorporated quadruple-drug regimens in the induction treatment of NDMM were not unanimous. We propose that aggregating outcomes from different clinical trials may resolve this debate. This meta-analysis was designed to compare the efficacy and safety of triple-drug regimens and daratumumab-incorporated quadruple-drug regimens in patients with NDMM.

Condition being studied Triple-drug regimens, including bortezomib-lenalidomide-dexamethasone (VRd) and bortezomib-melphalan-prednisone (VMP), are the most widely approved induction treatments for multiple myeloma (MM). VRd followed by autologous stem-cell transplantation, consolidation therapy with VRd, and maintenance therapy with lenalidomide is considered to be standard care for transplantation-eligible patients with newly diagnosed MM (NDMM). However, this approach is noncurative in the vast majority of patients.

METHODS

Search strategy Search strategy and terms in PubMed database

Research question as searched in PubMed on 05-12-2024
Daratumumab
(((((((((daratumumab[Title/Abstract]) OR Darzalex[Title/Abstract]) OR human CD38[Title/Abstract]) OR human-CD38[Title/Abstract]) OR humax CD38[Title/Abstract]) OR humax-CD38[Title/Abstract]) OR antiCD38[Title/Abstract]) OR anti CD38[Title/Abstract]) OR anti-CD38[Title/Abstract])
Multiple myeloma
("Multiple Myeloma"[Mesh]) OR ((((((((((((((((((Multiple Myelomas[Title/Abstract]) OR Myelomas, Multiple[Title/Abstract]) OR Myeloma, Multiple[Title/Abstract]) OR Myeloma, Plasma-Cell[Title/Abstract]) OR Myeloma, Plasma Cell[Title/

Abstract]) OR Myelomas, Plasma-Cell[Title/Abstract]) OR Plasma-Cell Myeloma[Title/Abstract]) OR Plasma-Cell Myelomas[Title/Abstract]) OR Myelomatosis[Title/Abstract]) OR Myelomatoses[Title/Abstract]) OR Plasma Cell Myeloma[Title/Abstract]) OR Cell Myeloma, Plasma[Title/Abstract]) OR Cell Myelomas, Plasma[Title/Abstract]) OR Myelomas, Plasma Cell[Title/Abstract]) OR Plasma Cell Myelomas[Title/Abstract]) OR Kahler Disease[Title/Abstract]) OR Disease, Kahler[Title/Abstract]) OR Myeloma-Multiple[Title/Abstract]) OR Myeloma Multiple[Title/Abstract])
Study
("randomized controlled trial"[pt] OR "controlled clinical trial"[pt] OR randomized[tiab] OR placebo[tiab] OR "drug therapy"[sh] OR randomly[tiab] OR trial[tiab] OR groups[tiab]) NOT (Meta-Analysis[ptyp] OR Review[ptyp] OR systematic[sb])
Limitations
((rat OR Rats OR Mouse OR Mice OR pig OR pigs OR cow OR cows OR sheep OR chicken* OR dog OR dogs) NOT human [mesh])

Combine: ("Daratumumab" AND "Multiple myeloma" AND "Study") NOT Limitations.

Participant or population patients with multiple myeloma.

Intervention daratumumab-incorporated quadruple-drug regimens versus triple-drug c regimens.

Comparator Not applicable.

Study designs to be included Randomized controlled trials (RCTs).

Eligibility criteria Selection Criteria
The studies identified were independently evaluated by two reviewers. Studies were included if they met the following inclusion criteria:
•research design: randomized controlled trials (RCTs);
•participants: patients with MM;
•intervention: daratumumab-incorporated quadruple-drug regimens versus triple-drug c regimens;
•outcomes: overall response rate (ORR), the rate of complete response (CR) or better (comprising CR and sCR), the rate of very good partial response (VGPR) or better (comprising VGPR, CR and sCR), the rate of negative status for MRD, PFS and toxicity events.

Information sources Two independent authors conducted a comprehensive search for relevant information using the PubMed, EMBASE, and Cochrane Library databases.not applicable.

Main outcome(s) Overall response rate (ORR), the rate of complete response (CR) or better (comprising CR and sCR), the rate of very good partial response (VGPR) or better (comprising VGPR, CR and sCR), the rate of negative status for MRD, PFS.

Additional outcome(s) Toxicity events.

Quality assessment / Risk of bias analysis Methodological quality of each study was assessed by two independent researchers. We adopted the Cochrane Collaboration Risk of Bias tool to judge the quality of RCTs.

Strategy of data synthesis Analyses were conducted using RevMan 5.4 and Stata 16.0. Heterogeneity across the included trials was assessed using the I^2 statistic. An I^2 value of 25% to 50% was considered to indicate low heterogeneity, 50% to 75% moderate heterogeneity, and greater than 75% high heterogeneity. A random effects model was applied when the I^2 value exceeded 50%, whereas a fixed effects model was used otherwise.

Subgroup analysis We introduced the subgroup analyses for PFS regarding patients' physical condition (transplant-ineligible NDMM subgroup and transplant-eligible NDMM subgroup) and backbone myeloma regimens (D-VMP/VMP, D-VTd/VTd, D-VRd/VRd and D-VCD/VCD subgroup).

Sensitivity analysis We introduced the sensitivity analysis to assess the influence of each study on the pooled outcomes by removing single trial each time in primary outcomes.

Country(ies) involved China.

Keywords daratumumab, Standard Triple-drug Regimens, Multiple Myeloma.

Contributions of each author
Author 1 - Bin Hu.
Author 2 - Dan Fang.
Author 3 - Jinxia Cao.
Author 4 - Tianqi Li.
Author 5 - Jun Wang.