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The addition of CD38 monoclonal antibody to triplet regimens improves survival in newly diagnosed multiple myeloma with high-risk cytogenetics: A systematic review and meta-analysis of randomized controlled trials

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ADMINISTRATIVE INFORMATION

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Review Stage at time of this submission - Data extraction.

Conflicts of interest - The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 26 October 2025 and was last updated on 26 October 2025.

INTRODUCTION

Review question / Objective The efficacy of CD38 monoclonal antibody (mAb)-based quadruplet regimens versus triplet regimens in newly diagnosed multiple myeloma (NDMM) patients with high-risk cytogenetics remains controversial. This meta-analysis aims to consolidate evidence from randomized controlled trials (RCTs) to resolve this clinical uncertainty.

Condition being studied Multiple myeloma is a malignant hematologic cancer characterized by the uncontrolled proliferation of plasma cells in the bone marrow. These aberrant cells accumulate, crowding out healthy blood cells and often producing abnormal antibodies. This can lead to clinical manifestations such as bone pain or fractures, anemia, renal impairment, and hypercalcemia. While currently considered incurable, the disease is treatable. Significant therapeutic advances, including novel agents and immunotherapies, have substantially improved survival rates and quality of life for patients, allowing many to manage it as a chronic condition.

METHODS

Participant or population Participants: newly diagnosed multiple myeloma patients with high-risk cytogenetics.

Intervention CD38 mAb-incorporated quadruplet regimens.

Comparator Traditional triplet regimens.

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

Eligibility criteria The identified studies underwent independent assessment by two reviewers.

Studies were included if they met the following criteria:
•research design: randomized controlled trials (RCTs);
•participants: NDMM patients with high-risk cytogenetics;
•intervention: CD38 mAb-incorporated quadruplet regimens versus triplet regimens;
•outcomes: the rate of negative status for MRD (10-5 threshold) and PFS.

Information sources Two independent investigators systematically performed literature searches across multiple electronic databases, including PubMed, EMBASE, and the Cochrane Library. The inclusion criteria were restricted to published randomized controlled trials with accessible full-text articles. To ensure comprehensive coverage, the reference lists of all eligible publications were manually examined to identify other potentially relevant studies. The search encompassed all available literature published through September 2025.

Main outcome(s) The objective was to compare the negative MRD status rate and PFS between the two arms.

Quality assessment / Risk of bias analysis The Cochrane Collaboration's Risk of Bias tool was utilized to assess the quality of the randomized controlled trials.

Strategy of data synthesis We will introduce RevMan 5.4 for analyses. Study heterogeneity was examined with the I^2 statistic, which interpreted values of 25%-50% as low, 50%-75% as moderate, and >75% as high. Based on the results, a random-effects model was implemented for I^2 scores exceeding 50%; if not, a fixed-effects model was chosen.

Subgroup analysis We will perform subgroup analyses of PFS based on the type of CD38 mAbs (daratumumab or isatuximab) and transplant eligibility (transplant-eligible or ineligible).

Sensitivity analysis We will introduce 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 All investigators involved in this study are from Mainland China.

Keywords CD38 monoclonal antibodies, quadruplet regimens, triplet regimens, multiple myeloma, meta-analysis.

Contributions of each author
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