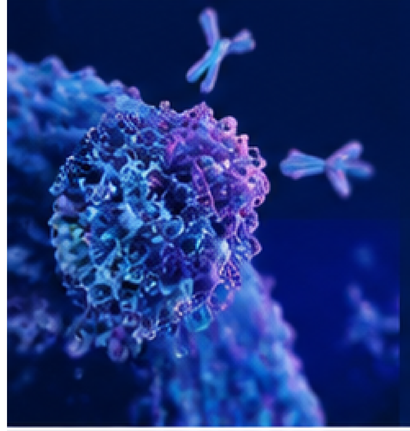

# Comparative Outcomes of CD38 Antibody-Containing Four-Drug Induction Strategies Versus Standard Triplet Therapy in High-Risk Newly Diagnosed Multiple Myeloma: A Systematic Review and Meta-Analysis


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9 RCTs
4,557 Patients Included


Keywords: CD38, Antbody, Therapy, Outcomes, Myeloma


## BACKGROUND

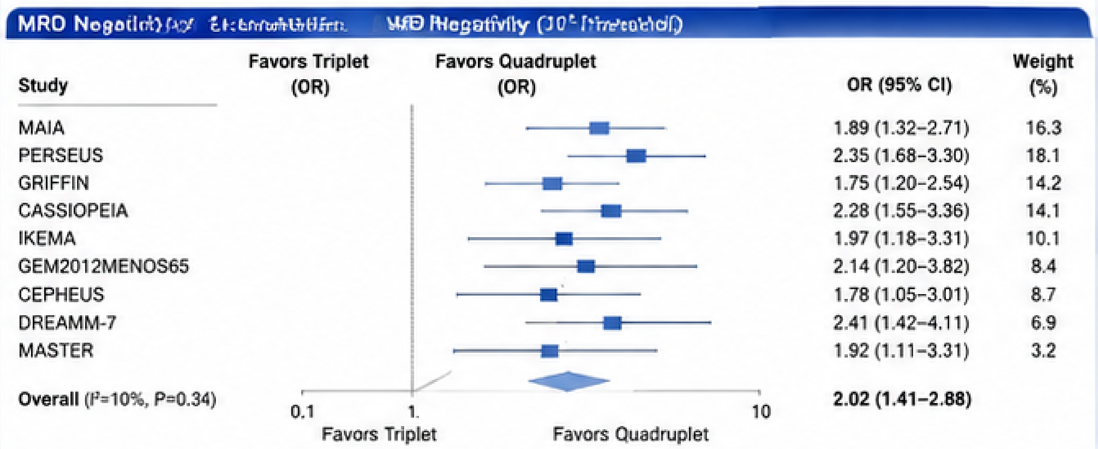
CD38 monoclonal antibody (mAb)-based quadruplet regimens have become a standard induction strategy for newly diagnosed multiple myeloma (NDMM). However, their benefit in patients with high-risk cytogenetic abnormalities remains uncertain. This systematic review and meta-analysis evaluated the efficacy of CD38 mAb-based quadruplet regimens compared with conventional triplet regimens in NDMM patients with high-risk cytogenetics.

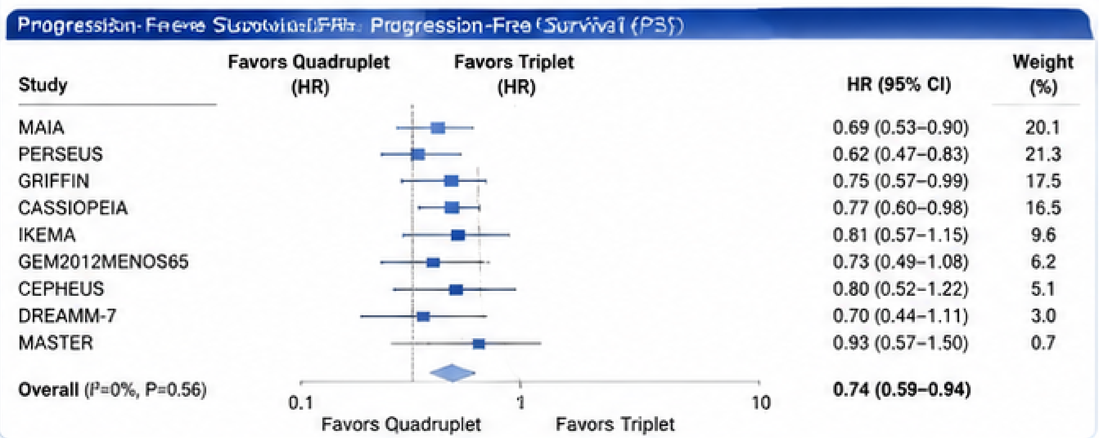
## METHODS

A systematic search of PubMed, EMBASE, and the Cochrane Library was conducted for randomized controlled trials (RCTs) published threugh October 2025. Eligible studies included NDMM patients with high-risk cytogenetic abnormalities receiving CD38 mAb-based quadruplet therapy versus triplet regimens. Primary outcomes were measurable residual disease (MRD) negativity at the $10^{-5}$ threshold and progression-free survival (PFS). Odds ratios (ORs) and hazard ratios (HRs) with 95% confidence intervals (CIs) were pooled using random-effects models. Subgroup and sensitivity analyses were performed according to CD38 mab type and transplant eligibility.

## RESULTS

Nine RCTs comprising 4,557 patients were included. Compared with triplet therapy, CD38 mAb-based quadruplet regimens significantly improved MRD negativity (pooled OR=2.02, 95% CI: 1.41–2.88, P=0.0001; $I^2$=10%) and prolonged PFS (pooled HR=0.74, 95% CI: 0.59–0.94, P=0.01; $I^2$=0%).




## SUBGROUP ANALYSES FOR PFS

### By CD38 mAb Type

| Subgroup | HR (95% CI) | P value |
|---|---|---|
| Daratumumab-based quadruplets | 0.68 (0.53–0.87) | 0.002 |
| Isatuximab-based quadruplets | 1.04 (0.67–1.62) | 0.84 |
| **P for subgroup difference** | | **0.01** |

### By Transplant Eligibility

| Subgroup | HR (95% CI) | P value |
|---|---|---|
| Transplant-eligible | 0.66 (0.51–0.85) | 0.001 |
| Transplant-ineligible | 0.79 (0.56–1.13) | 0.19 |
| **P for subgroup difference** | | **0.08** |

Sensitivity analyses confirmed the robustness of MRD findings; however, exclusion of the PERSEUS trial attenuated the PFS benefit.

## CONCLUSIONS

CD38 mAb-based quadruplet regimens significantly enhance MRD negativity and improve PFS in NDMM patients with high-risk cytogenetics, particularly among transplant-eligible populations and daratumumab-containing regimens. These findings support the incorporation of CD38 mAb-based quadruplets into frontline treatment strategies for selected high-risk NDMM patients.

**Abbreviations:** mAb, monoclonal antibody; NDMM, newly diagonsed multiple myeloma; MRD, measurable residual disease; PFS, progression-free survival; OR, odds ratio; HR, hazard ratio; CI, confidence interval; RCT, randomized controlled trial.

Search through October 2025