Does Minimal Residual Disease Negativity Overcome High-Risk Cytogenetics After Autologous Stem Cell Transplantation in Multiple Myeloma?

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1 Context

Minimal residual disease (MRD) negativity has become an important marker of depth of response in multiple myeloma. However, it remains unclear whether achieving MRD negativity after transplant can offset the poorer outcomes typically seen in patients with high-risk cytogenetic abnormalities.

2 Objective

To assess whether MRD negativity improves survival outcomes independently of cytogenetic risk in patients undergoing autologous stem cell transplantation. This distinction is central to how post-transplant risk is communicated and how maintenance strategies are chosen.

3 Design

We performed a systematic review and meta-analysis in accordance with PRISMA 2020 guidelines. PubMed, Embase, Web of Science, and Cochrane Library were searched from 2010 through March 2026. Hazard ratios (HRs) for progression-free survival (PFS) and overall survival (OS) were pooled using random-effects models, with heterogeneity quantified via the I^2 statistic and subgroup analyses based on cytogenetic risk.

4 Setting

Multicentre clinical trials and real-world cohort studies evaluating MRD status after autologous transplantation, reflecting both controlled-trial populations and routine clinical practice.

5 Participants

Studies including patients with newly diagnosed multiple myeloma undergoing autologous transplantation with available MRD and cytogenetic data were included. High-risk cytogenetics were defined by abnormalities such as del(17p), t(4;14), t(14;16), and 1q gain. Across included studies, approximately 13,000 patients were analysed.

6 Interventions

Standard induction therapy followed by autologous stem cell transplantation, with most cohorts incorporating maintenance therapy — consistent with contemporary standard-of-care management of newly diagnosed multiple myeloma.

7 Main Outcome Measures

Progression-free survival and overall survival based on MRD status within cytogenetic risk groups, compared to determine whether MRD negativity narrows the survival gap driven by adverse cytogenetics.

Results

HR 0.31

improved PFS with MRD negativity (95% CI 0.20–0.48; I^2=0%)

~13,000

patients analysed across pooled studies

HR 2.8–4.2

for progression when MRD remains positive

- MRD-negative patients consistently had better outcomes than MRD-positive patients, across cytogenetic risk groups.
- Low between-study heterogeneity (I^2=0%) supported the consistency of the pooled PFS estimate.
- MRD negativity improved outcomes even among patients with high-risk cytogenetics.
- However, MRD-negative high-risk patients still had inferior outcomes versus MRD-negative standard-risk patients — the adverse biology was not fully overcome.
- MRD positivity was independently associated with worse outcomes for both PFS and OS across individual studies.

Conclusions

MRD negativity after autologous transplantation is associated with improved outcomes in multiple myeloma, including in patients with high-risk cytogenetics — but it does not completely overcome the adverse prognosis of high-risk disease.

These findings support integrating MRD status with cytogenetic risk when making post-transplant treatment decisions. By pooling data across roughly 13,000 patients, this analysis shows that depth of response and cytogenetic risk are complementary — not interchangeable — prognostic tools.

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