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Efficacy of Isatuximab-Based Regimens Compared to Standard of Care in Transplant-Eligible Newly Diagnosed Multiple Myeloma: A Meta-Analysis of Phase III Clinical Trials

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INTRODUCTION

In multiple myeloma (MM), plasma cells, including malignant cells, express CD-38 glycoprotein, which is the target for isatuximab (Isa), an IgG1k monoclonal antibody approved for MM treatment.(1)

METHOD

- To assess the efficacy of Isa addition to the standard of care regimens in newly diagnosed (ND) transplant-eligible (TE) MM patients.

METHODS

- We conducted a comprehensive literature search on PubMed, EMBASE, Cochrane, and ClinicalTrials.gov through April 2024.
- Our search strategy included MeSH terms and keywords for multiple myeloma, isatuximab, and Sarclisa.
- Initial search yielded 351 articles. After excluding duplicates, review articles, and non-relevant articles, we included two phase III randomized clinical trials (RCTs) reporting efficacy of Isa addition to the standard of care in TE-NDMM.
- Odds ratio (OR) of complete response (CR), very good partial response (VGPR), and minimal residual disease (MRD) negative status were computed along with a 95% confidence interval (CI) and p-value for pooled analysis using fixed effect model in RevMan v.5.4

RESULTS

- Two phase III RCTs (GMMG-HD7 and IsKia), including 960 patients with TE-NDMM, were eligible. IsKia and GMMG-HD7 compared Isa-carfilzomib-lenalidomide-dexamethasone (IsaKRd) (n=151) vs. KRd (n=151), and Isa-lenalidomide-bortezomib-dexamethasone (IsaRVd) (n=330) vs RVd (n=328), respectively.
- Isa dose was 10mg/kg in both studies, and the median follow-up was 20 months in IsKia and 23 months in GMMG-HD7 clinical trial.
- A pooled analysis showed a significant achievement of MRD negative status in Isa-based regimens compared to the control group (OR: 1.98, 95%CI: 1.38-2.95, p<0.05, I2=0). Isa addition to the standard of care regimen (KRd, RVd) also proved to be of improved efficacy as compared to the control group in the pooled analysis, i.e., CR (OR:1.14, 95%CI: 0.73–1.80, p = 0.56, I2=26), VGPR (OR: 1.87, 95%CI: 1.09-3.21, p < 0.05, I2=30).
- However, Isa-based regimens increased the risk of neutropenia [relative risk (RR): 1.62, 95%CI: 1.14-2.28, p < 0.05, I2=0] and infections (RR: 1.32, 95%CI: 0.79-2.21, p = 0.30, I2=0) compared to control group.

CONCLUSIONS

Isa addition to standard of care regimens (KRd, RVd) for TE-NDMM, achieved surrogate endpoints with improved efficacy in terms of VGPR, CR, and MRD negative status with manageable toxicity, providing a benchmark for future studies.

REFERENCES

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