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651.MULTIPLE MYELOMA AND PLASMA CELL DYSCRASIAS: BASIC AND TRANSLATIONAL

Evidence-Based Recommendations for Induction Treatment of Newly Diagnosed Transplant-Eligible Multiple Myeloma Patients; A Scoping Review

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Introduction

Multiple myeloma is a hematological malignancy characterized by the uncontrolled proliferation of plasma cells within the bone marrow, with an increasing incidence and mortality in the last decade. Eligibility for stem cell transplantation plays a crucial role in determining the approach to treatment, with transplant eligible patients undergoing triple induction therapy with an immunomodulatory agent, a proteasome inhibitor, and steroid. We aimed to review the recent data on the available treatment options for newly diagnosed multiple myeloma (NDMM) in transplant eligible patients.

Methods

A scoping review was conducted according to the PRISMA 2020 guidelines utilizing the PubMed and Embase databases. The inclusion criteria was phase II or III clinical trials pertaining to the use of triple and quadruple therapy in NDMM patients, from the year 2010 onwards. A total of 2377 search results were screened, with 510 undergoing full-text screening against the inclusion criteria. Covidence was used to facilitate the screening process (Figure 1).

Results

Forty studies were included in the analysis. Eleven trials were based on Daratumumab induction. Additionally, two trials each utilized Isatuximab and Carfilzomib-based induction. One trial employed induction therapy containing Elotuzumab, and another utilized Cyclophosphamide. Addition of Daratumumab to the triplet regimen resulted in significant improvements in response rates and depth of responses. CASSIOPEIA trial demonstrated a notable improvement in minimal residual disease (MRD), with VTd treatment yielding 44% MRD, while Dara-VTd regimens achieved 64% MRD. Similarly, complete response (CR) rates increased from 26% to 39%, respectively. GRIFFIN trial revealed a remarkable 55% reduction in the risk of disease progression for patients with Dara-RVd . Moreover, the estimated 48-month progression-free survival (PFS) rate was 87.2% in the Dara-RVd group, compared to 70% in the RVd group. Notably, the median PFS was not reached in either treatment arm. The Lyra trial, which analyzed Dara-CyBorD followed by Dara maintenance, demonstrated a CR rate of 48.7% for transplant patients and 29.8% for non-transplant patients, respectively. Additionally, the MASTER trial revealed that Dara-KRd/autologous hematopoietic cell transplant (AHCT) led to a high rate of MRD negativity, with 80% of patients achieving MRD negativity. The two-year PFS was 87%. Furthermore, the addition of Isatuximab and Carfilzomib to the treatment regimen demonstrated favorable outcomes in terms of MRD and PFS (Table 1).

The addition of Elotuzumab did not lead to a significant improvement in outcomes. Moreover, caution is warranted when using Cyclophosphamide, given its less favorable safety profile and limited additional benefit in survival outcomes (MRD: 27% in +Cyclophosphamide arm vs. 35% without), including a temporary decline in health-related quality of life.

Conclusion

In conclusion, this scoping review underscores the significance of individualized treatment approaches for multiple myeloma based on clinical trial results. Each induction regimen has shown varying levels of efficacy and safety, offering clinicians flexibility to tailor treatments for different patient populations. The results from these trials will serve as valuable benchmarks and inform future research in the quest for improved therapies for NDMM patients.

Disclosures No relevant conflicts of interest to declare.

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Table 1. Quadruplet Induction Therapies

Authors	Study	Treatment	Outcomes	Median Follow Up
Induction therapy containing Daratumumab:				
Costa, L. J.; Chhabra, S.	Master Trial, 2022	Dara-KRd	2 y PFS: 87% MRD: 80%	25.1 months
Moreau P.; Attal M.;	CASSIOPEIA, 2019	Dara-VTd vs VTd	mPFS: Not reached MRD: 64% vs 44%	35.4 months
Sonneveld P.; Attal M.; Perrot A.	NCT02541383 trial (CASSIOPEIA based), 2020	Dara-VTd vs VTd	sCR: 28.9% vs 20.3%	35.4 months
Rifkin, R.; Melear, J.	LYRA, 2021	Dara-VCd	36-mos PFS: NDMM w ASCT (69.3%), NDMM w/o ASCT (72.6%) VGPR: NDMM w ASCT (82.1%), NDMM w/o ASCT (70.2%)	35.7 months
Voorhees P.M.; Kaufman J.L.	GRIFFIN, 2022	Dara-RVd vs RVd	MRD 64% vs. 30% 48-month PFS: 87.2% vs 70%	49.6 months
Induction therapy containing Isatuximab:				
Goldschmidt, H.; Mai, E. K.; Bertsch, U	GMMG-HD7 (NCT03617731), 2022	Isa-VRd vs VRd	MRD 50% vs 36%	125 days
Induction therapy containing Carfilzomib				
Jackson G.H.; Pawlyn C.	Myeloma XI+, 2021	KRdc vs Rdc/Tdc	MRD: for KRDc 55% post induction and KRDc 75% post ASCT VGPR: 82.3% vs 58.9% CR: 31% vs 24%	34.5 months
Induction therapy containing Elotuzumab				
Usmani, S. Z.; Hoering, A	SWOG-1211, 2021	Elotuzumab VRd vs VRd	mPFS 31.47% vs 33.64% OS: 68mo vs not attained	53 months
Induction therapy containing Cyclophosphamide				
Ludwig, H.; Greil, R	Ludwig's study (NCT00531453, 2015)	VTdc vs VTd	mPFS 36.3 vs 56.3 3-year OS: 83.7% vs 79.6% 5-year OS: 65.3% vs 69.1% MRD: 27% vs 35%	64.8 months

ASCT: autologous stem-cell transplantation, PFS: progression-free survival; mPFS: median progression-free survival, MRD: minimal residual disease, sCR: stringent complete response, CR: Complete response, VGPR: very good partial response; OS: overall survival

Bortezomib, thalidomide, dexamethasone (Vtd); daratumumab plus lenalidomide, bortezomib, dexamethasone (D-RVd); daratumumab, cyclophosphamide, bortezomib and dexamethasone (Dara-CyBorD); daratumumab, lenalidomide, and dexamethasone (Dara-KRd)

Figure 1. PRISMA flowchart of included articles

Figure 1