Impact of Induction with VRD Vs. VCD on the Outcome of Patients with Multiple Myeloma after an Autologous Hematopoietic Stem Cell Transplantation

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INTRODUCTION

Induction therapy with a triplet regimen, followed by high dose therapy and autologous hematopoietic stem cell transplantation (auto-HCT) is the standard of care for newly diagnosed transplant-eligible patients with multiple myeloma.

Various bortezomib-based combinations have been used, with bortezomib- dexamethasone with either lenalidomide (VRD) or cyclophosphamide (VCD) being the most common regimens.

In the EVOLUTION trial, there was a higher pre-transplant response rate with VRD, but no difference in 1-year progression-free survival (PFS) or overall survival (OS) between the two regimens[1]. Two retrospective studies comparing VRD and VCD showed disparate results [2,3].

With this background, we conducted this single-center, retrospective analysis to compare the outcomes of VRD vs. VCD in newly diagnosed MM patients who underwent auto-HCT at our institution.

MATERIALS AND METHODS

- We identified 323 consecutive patients who received VRD or VCD as induction before auto-HCT.
- All patients received melphalan as a conditioning regimen and single-agent lenalidomide as maintenance therapy.
- Primary endpoints were complete response (CR) rates, PFS and OS.

RESULTS

- The median follow-up from auto-HCT was 64.5 (range, 4 to 149), and 71 (range, 12 to 130) months in the VRD and VCD groups, respectively.
- The median interval between auto-HCT and the start of maintenance therapy was 4 (range, 1 to 47), and 4 (range, 2 to 36) months in the VRD and VCD groups, respectively (p=0.78).

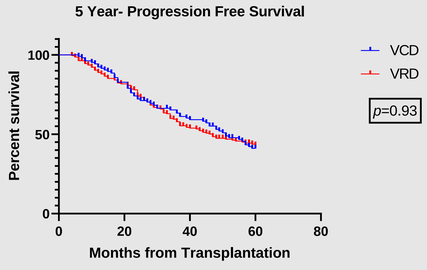
RESULTS

- There were no significant differences in baseline characteristics between the 2 induction groups, except for patients in the VCD group had:
  - ❑ Higher baseline serum creatinine level
  - ❑ Higher serum beta-2 microglobulin level
  - ❑ More patients with International Staging System (ISS) III disease
- The 100-day non-relapse mortality (NRM) was 0% in both induction groups.
- Twenty-five (11%) and 4 (4%) patients achieved a complete response (CR) before auto-HCT in the VRD and VCD groups, respectively (p=0.023).

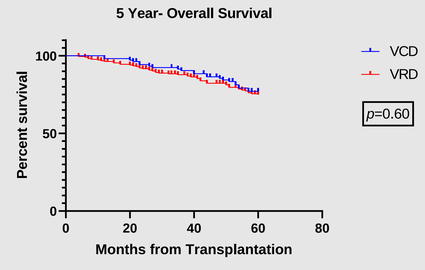
Characteristics

Characteristics	VRD (N= 218)	VCD (N= 105)	*p*-value
Median age, y (range)	62 (33-79)	59 (38-79)	0.06
Male, n (%)	115 (53)	54 (51)	0.90
Light chain type			0.80
Kappa	131 (61)	65 (62.5)	
Lambda	85 (39)	39 (37.5)	
Myeloma type, n (%)			0.75
IgG	134 (61)	62 (59)	
IgA	36 (17)	21 (20)	
Light Chain only	37 (17)	19 (18)	
Others	11 (5)	3 (3)	
Risk genetic abnormalities			0.58
Standard- risk	143 (66)	68 (65)	
High-risk	25 (11)	15 (14)	
Not available	50 (23)	22 (21)	
Creatinine level (mg/dl), median (range)	1 (0.47-13.6)	1.2 (0.6-28.5)	**0.001**
< 1.5	170 (82)	65 (64)	
≥ 1.5	37 (18)	36 (36)	
Melphalan dose (mg/m²)			0.82
140	17 (8)	9 (9)	
200	201 (92)	96 (91)	
International Staging System (ISS)			0.08
I	88 (40.5)	37 (35)	
II	51 (23.5)	22 (21)	
III	46 (21)	36 (34)	
Unknown	33 (15)	10 (10)	
Revised-ISS			**0.04**
I	56 (26)	16 (15)	
II	75 (34)	48 (46)	
III	14 (6)	9 (9)	
Unknown	73 (34)	32 (30)	

5-year Progression Free Survival in VRD vs. VCD induction



5-year Overall Survival in VRD vs. VCD induction



- One-hundred and seventeen (54%) and 55 (52%) patients achieved at least a very good partial response (VGPR) before auto-HCT in the VRD and VCD groups, respectively (p=0.90).
- At the last follow up, post-auto-HCT, 113 (52%) and 37 (35%) patients had achieved a CR in the VRD and VCD groups, respectively (p=0.006).
- Similarly, 186 (85%) and 97 (92%) patients had achieved at least a VGPR in the VRD and VCD groups, respectively (p=0.074).
- The 5-year PFS was 43% and 41% in VRD, and VCD group, respectively (p=0.93) (Figure 1A).
- The 5-year overall survival (OS) was 75% and 77% in VRD, and VCD group, respectively (p=0.60) (Figure 1B).
- On multivariate analysis, achieving a CR post-auto-HCT was associated with a better PFS (p<0.0001; hazard ratio, .43; 95% CI, .27 to .66) and OS (p<0.0001; hazard ratio, .22; 95% CI, .11 to .46).

CONCLUSIONS

✓In this single-center retrospective analysis, induction therapy with VRD was associated with a higher CR rate, but there was no difference in PFS or OS between the two regimens.

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Disclosure

The authors declare no competing financial interests.