Real-world experience of induction therapy for treatment of newly diagnosed multiple myeloma: an analysis from the Australian and New Zealand, and the Asia-Pacific Myeloma and Related Diseases Registries

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BACKGROUND

Until 2019, bortezomib, cyclophosphamide and dexamethasone (VCd) was the most commonly used induction treatment regimen in Australia for transplant eligible patients with newly diagnosed multiple myeloma (NDMM)[1, 2]. Since June 2020, the addition of bortezomib, lenalidomide and dexamethasone (VRd) onto the Pharmaceutical Benefits Scheme (PBS) for induction therapy has allowed clinicians to access lenalidomide, and thus increase its use for patients with NDMM[3].

Another induction regimen commonly used in multiple jurisdictions is bortezomib, thalidomide and dexamethasone (VTd)[4]. However, the use in Australia has been limited by the absence of thalidomide on the PBS. All three lines of induction therapy have high overall response rates (ORR; ≥ partial response) and rates of achieving a very good partial response (VGPR). We aimed to evaluate the real world experience (RWE) with these induction regimens for NDMM patients in the Australian, New Zealand (ANZ) and Asian Pacific (APAC) region.

METHOD

We analysed all patients aged ≥ 18 years with NDMM, commencing induction therapy with either VCd, VTd or VRd between January 2016 and December 2021, using data from the ANZ and the APAC Myeloma and Related Diseases Registries (MRDR). Both autologous stem cell transplant (ASCT) eligible and ineligible patients were included. Baseline patient characteristics were collected, including age, sex, country of treatment and risk category at diagnosis (R-ISS and International Myeloma Working Group (IMWG) criteria). Progression-free survival (PFS), overall survival (OS), ORR were assessed. PFS and OS were estimated using Kaplan-Meier methods. Median follow up duration data were also collected.

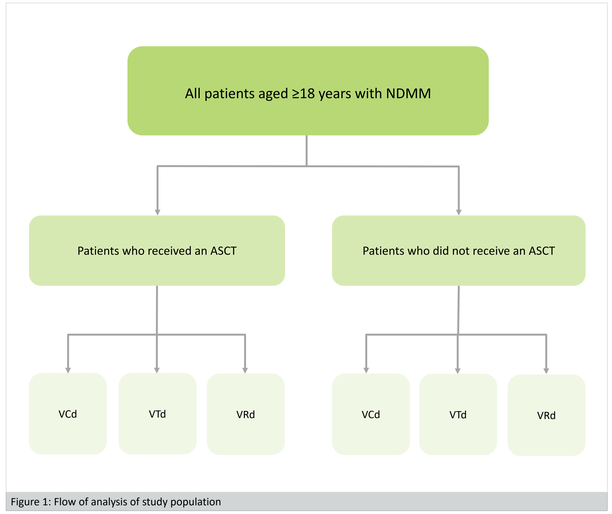

Figure 1: Flow of analysis of study population

RESULTS

2939 patients were included in the analysis. The baseline characteristics of the study population are summarised in Table 1. The proportion of patients undergoing an ASCT differed between the 3 induction cohorts - VCd 56.4%, VTd 75.1% and VRd 58.3% (p-value < 0.001).

In the ASCT group, ORRs were VCd 85.8%, VTd 98.1% and VRd 94.7% (p-value < 0.001). Kaplan-Meier survival curves showed a statistically significant difference between treatments in PFS with VRd having the longest PFS, followed by VCd and VTd. There was no difference in OS between the induction treatments. PFS advantage for VRd in ASCT patients remained when adjusted for country - hazard ratio (95% CI) with VCd as reference: VTd 1.46 (0.64-3.37) p = 0.37, VRd 0.61 (0.37-0.99) p = 0.044.

In patients who did not have an ASCT, ORRs were VCd 83.3%, VTd 87.8% and VRd 92.9% (p-value 0.049). No differences were seen for PFS and OS between induction treatments.

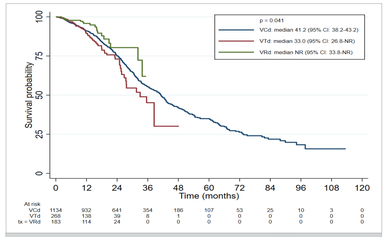

Figure 2: Progression-free survival of patients receiving ASCT

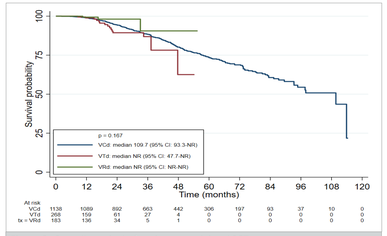

Figure 3: Overall survival of patients receiving ASCT

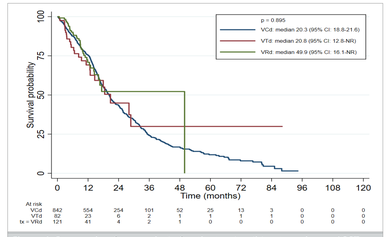

Figure 4: Progression-free survival of patients who did not receive an ASCT

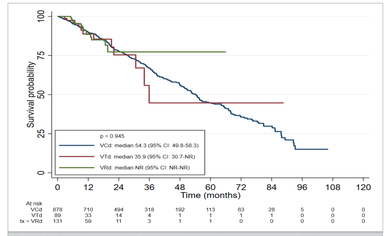

Figure 5: Overall survival of patients who did not receive an ASCT

Table 2: Comparison of induction treatment regimens and responses from patients that received an ASCT

	VCd (N = 1138)	VTd (N = 268)	VRd (N = 183)	P-value
Overall response rate^	857/999 (85.8%)	258/263 (98.1%)	144/152 (94.7%)	< 0.001
Best clinical response to chemotherapy^				< 0.001
Complete remission	103/999 (10.3%)	47/263 (17.9%)	44/152 (28.9%)	
Very good partial response	294/999 (29.4%)	175/263 (66.5%)	55/152 (36.2%)	
Partial response	460/999 (46.0%)	36/263 (13.7%)	45/152 (29.6%)	
Minimal response	98/999 (9.8%)	2/263 (0.8%)	7/152 (4.6%)	
Stable disease	27/999 (2.7%)	1/263 (0.4%)	1/152 (0.7%)	
Progressive disease	17/999 (1.7%)	2/263 (0.8%)	0/152 (0.0%)	
Median time to treatment in weeks (IQR)	2.4 (1.0-4.4)	1.1 (0.3-2.6)	3.1 (1.6-4.7)	< 0.001
Median follow-up (months)	44.32	14.42	15.41	

^Only includes patients with a documented response to chemotherapy (VCd = 999, VTd = 263, VRd = 152)

Table 3: Comparison of induction treatment regimens and responses from patients that did not receive an ASCT

	VCd (N = 878)	VTd (N = 89)	VRd (N = 131)	P-value
Overall response rate^	579/695 (83.3%)	65/74 (87.8%)	79/85 (92.9%)	0.049
Best clinical response to chemotherapy				0.008
Complete remission	87/695 (12.5%)	12/74 (16.2%)	21/85 (24.7%)	
Very good partial response	226/695 (32.5%)	33/74 (44.6%)	30/85 (35.3%)	
Partial response	266/695 (38.3%)	20/74 (27.0%)	28/85 (32.9%)	
Minimal response	69/695 (9.9%)	3/74 (4.1%)	2/85 (2.4%)	
Stable disease	26/695 (3.7%)	5/74 (6.8%)	3/85 (3.5%)	
Progressive disease	21/695 (3.0%)	1/74 (1.4%)	1/85 (1.2%)	
Median time to treatment in weeks (IQR)	2.6 (1.0-5.0)	1.4 (0.4-3.3)	2.9 (1.1-5.0)	0.001
Median follow-up (months)	36.3	8.44	12.32	

^Only includes patients with a documented response to chemotherapy (VCd = 695, VTd = 74, VRd = 85)

RESULTS

Table 1: Baseline characteristics of the patients

	VCd (N = 2107)	VTd (N = 385)	VRd (N = 447)	P-value
Median age (IQR)	65.3 (57.8-72.1)	60.8 (54.9-65.1)	64.9 (56.2-70.6)	< 0.001
Age > 70	653/2107 (31%)	13/385 (3.4%)	128/447 (28.6%)	< 0.001
Sex				0.051
Male	1296/2105 (61.6%)	212/385 (55.1%)	275/446 (61.7%)	
Female	809/2105 (38.4%)	173/385 (44.9%)	171/446 (38.3%)	
Did the patient receive ASCT^	1138/2016 (56.4%)	268/357 (75.1%)	183/314 (58.3%)	< 0.001
Country				< 0.001
Australia	1445/2107 (68.6%)	9/385 (2.3%)	379/447 (84.8%)	
New Zealand	625/2107 (29.7%)	4/385 (1.0%)	3/447 (0.7%)	
Korea	3/2107 (0.1%)	350/385 (90.9%)	41/447 (9.2%)	
Singapore	23/2107 (1.1%)	20/385 (5.2%)	24/447 (5.4%)	
Malaysia	11/2107 (0.5%)	2/385 (0.5%)	0/447 (0.0%)	
Revised ISS (calculated)				< 0.001
1	142/1171 (12.1%)	51/328 (15.5%)	61/286 (21.3%)	
2	875/1171 (74.7%)	207/328 (63.1%)	194/286 (67.8%)	
3	154 (1171 (13.2%)	70/328 (21.3%)	31/286 (10.8%)	
IMWG risk category (calculated)				< 0.001
Low	168/975 (17.2%)	60/301 (19.9%)	62/253 (24.5%)	
Moderate	695/975 (71.3%)	164/301 (54.5%)	147/253 (58.1%)	
High	112/975 (11.5%)	77/301 (25.6%)	44/253 (17.4%)	

^Only includes patients at least 12 months post diagnosis and have follow-up data

CONCLUSION

For ASCT patients VRd appears to confer longer PFS than VCd or VTd, but not in OS. In patients not receiving an ASCT, there was no difference in PFS or OS between therapies. Regional differences in treatment patterns may confound results.

REFERENCES

1. Quach et al. Clinical Practice Guideline Multiple Myeloma. Myeloma Australia 2019.

2. Mai EK et al. Phase III trial of bortezomib, cyclophosphamide and dexamethasone (VCD) versus bortezomib, doxorubicin and dexamethasone (PAd) in newly diagnosed myeloma. Leukemia. 2015 Aug 1;29(8):1721–9.

3. Durie BGM et al. Bortezomib with lenalidomide and dexamethasone versus lenalidomide and dexamethasone alone in patients with newly diagnosed myeloma without intent for immediate autologous stem-cell transplant (SWOG S0777): a randomised, open-label, phase 3 trial. The Lancet. 2017 Feb 4;389(10068):519–27.

4. Moreau P et al. VTD is superior to VCD prior to intensive therapy in multiple myeloma: results of the prospective IFM2013-04 trial. Blood. 2016 May 26;127(21):2569–74.

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