Real-world outcomes with bortezomib-containing regimens and lenalidomide and dexamethasone for the treatment of transplant ineligible MM patients: A multi-institutional report from the National Myeloma Canada Research Network (MCRN) database

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Introduction

Bortezomib-containing regimens (BCRs) have been the standard frontline approach for the treatment of transplant ineligible multiple myeloma (TIMM) patients in Canada for many years.Recently, lenalidomide and dexamethasone (Ld) has become another funded option in Canada in the same therapeutic space. We aimed to compare the effect of BCRs and Ld for the treatment of TIMM using the newly-formed Myeloma Canada Research Network Multiple Myeloma Database (MCRN-MM-DB) project. This web-based centralized platform can track and characterize real-world outcomes of patients treated at major Canadian institutions and includes both legacy data dating back to 2007 (from 4 centres) as well as ongoing prospective data collection (from 11 centres) analyzed up to 01/07/18.

Methods

The primary objective was to assess the ORR, PFS and OS for TIMM patients treated with CyBorD/CyBorP, Ld, VMP (Bortezomib weekly) or VD/VP, each given as reported previously but with dose-adjustments at the discretion of the treating physician to maintain patients on therapy. Survival curves were constructed according to the Kaplan-Meier method and compared using the log rank test; a p value of <0.05 was considered significant.

Results

A total of 842 TIMM patients were evaluated. Clinical characteristics are shown in Table 1. Median OS and PFS for the entire cohort were 54.1 and 20.4 months, respectively. ORR and ≥VGPR rates were 83% and 52% for the entire cohort. A ≥VGPR rate of 53%, 46%, 56% and 51% were observed for patients treated with CyBorD/P, VMP, Ld and VD/VP, respectively (p=0.3). The median PFS was longer for Ld patients (25 months) compared to CyBorD/CyBorP, VMP and Vd/VP (19.3, 20.5 and 13.7 months, respectively), (p=0.03, Fig 1a). Patients were not matched and a lower creatinine value in the LD group compared to VD, CyBorD and VMP was noted (p=0.001).

Results

There was no significant difference in PFS between the 2 different alkylating-agent containing regimens when combined with bortezomib + steroids (CyBorD/P vs VMP, p =0.9). Further, median PFS was better in the group treated with LD compared to CyBorD/CyBorP. Median OS was 51, 59.5, 29.4 and 66.5 months for those patients treated with CyBorD/CyBorP, VMP, VD/VP and Ld, respectively (p=0.07, Fig 1b). OS was similar between CyBorD/CyBorP and VMP regimens (p=0.5). However, there was a trend of better OS for the grouop treated with RD compared to CyBorD/CyBorP.

Table 1. Clinical characteristics of TIMM patients at diagnosis from the Canadian National MCRN Database

Clinical Characteristics	All Patients (N=842)	CyBorD/P (N=423)	VMP (N=204)	Ld (N=160)	VD/VP (N=55)
Median Age (years)	73	71	74	75	70
Female (%)	42	39	46	44	44
Median Creat (umol/L) n=717	103	110	102	93	99
ISS Stage III (%) n=574	48	54	40	41	41
Plasma Cells (%) n=672	40	40	50	40	37
Median duration on Tx (months)	7.3	6.4	9.0	16.3	3.8

Ab: CyBorD; Cyclophosphamide, bortezomib and dexamethasone; CyBorP: cyclophosphamide,bortezomib and prednisone; VMP: bortezomib, melphalan and prednisone; VD: bortezomib and dexamethasone; VP: bortezomib and prednisone; Ld:lenalidomide and dexamethasone; Creat: Serum creatinine; N: Number of evaluable patients; Tx: Treatment

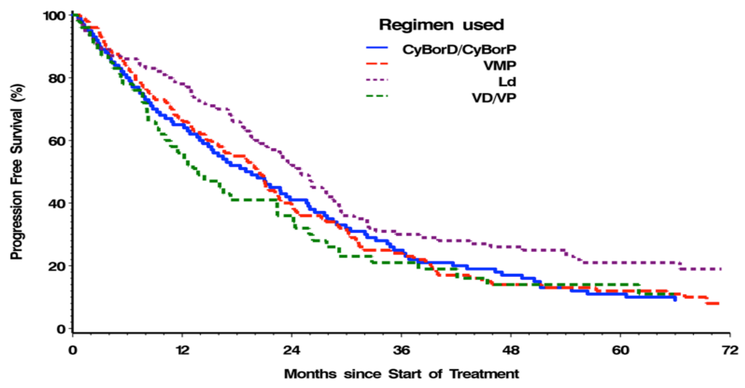

Figure 1a. Progression-free survival according to treatment regimen. The median PFS was longer for Ld patients (25 months) compared to CyBorD/CyBorP, VMP and Vd/VP, 19.3, 20.5 and 13.7 months respectively (p=0.03)

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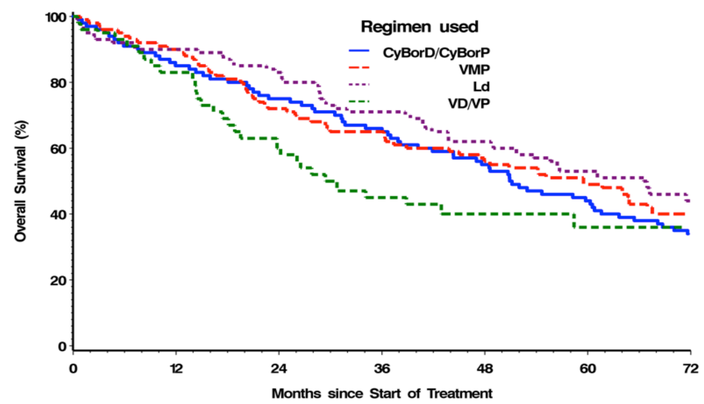

Figure 1b. Overall survival according to treatment regimen. Median OS was 51, 59.5, 29.4 and 66.5 months for patients treated with CyBorD/CyBorP, VMP, VD/VP and Ld respectively (p=0.07)

Median PFS			
Regimen_Name	Median	95% CI	
		[Lower	Upper)
CyBorD/CyBorP	19.364	16.340	21.929
RD	25.019	20.482	28.537

P=0.008

Median OS			
Regimen_Name	Median	95% CI	
		[Lower	Upper)
CyBorD/CyBorP	51.058	47.014	60.526
RD	66.510	48.986	87.288

P=0.08

Conclusions

1) This study confirms the utility of a large comprehensive national database to benchmark current results for comparison with newer regimens.
2) OS was not significantly different in patients treated with either a bortezomib-containing triplet (with an alkylator + steroid backbone) compared to continuous Ld as frontline therapy.
3) The BCR triplets and Ld were more efficacious than the bortezomib + steroid doublet (VD/VP) for both OS and PFS although, the small sample size and adverse factors, such as frailty and comorbidities, may have influenced the findings.
4) The median PFS in the range of 1.5-2 years and median OS of 4.5-5.5 years in this real-world cohort supports existing Phase III data and confirms triplet-based BCRs and Ld as valid standards of care for frontline therapy in TIMM. A trend to better PFS was observed in favor of the LD group. However, treatment durations were different among both regimens.