BP-013

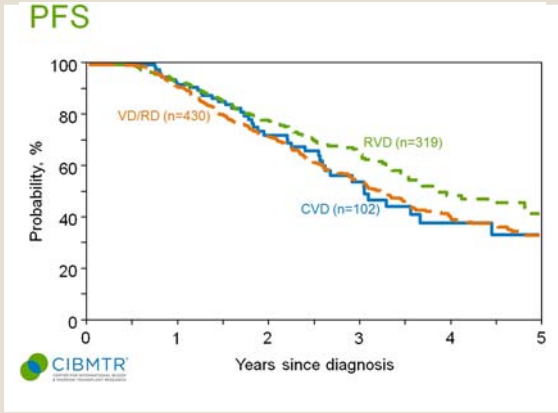
Induction regimens for autologous transplant (AHCT) eligible myeloma (MM) patients (pts) – Doublets or Triplets and Which Triplet?

P. Hari,[1] R.F. Cornell,[2] M.J. Zhang,[1] J. Huang,[1] A. Kassim,[2] L. Costa,[3] R.D. Innis-Shelton,[3] T. Mark,[4] Y.L. Nieto,[5] C. Gasparetto,[6] A. Krishnan,[7] A. D'Souza[1]

[1]Center for International Blood and Marrow Transplant Research (CIBMTR), Medical College of Wisconsin, Milwaukee, WI; [2]Vanderbilt University Medical Center, Nashville, TN; [3]University of Alabama-Birmingham, Birmingham, AL; [4]Weill Cornell Medical College, New York, NY; [5]MD Anderson Cancer Center, Houston, TX; [6]Duke University Medical Center, Durham, NC; [7]City of Hope Departments of Hematology and Hematopoietic Cell Transplantation, City of Hope, Duarte, CA

Introduction: Triplet regimens using bortezomib (V), dexamethasone (D) and lenalidomide (R) or cyclophosphamide (C) are most common current regimens for induction in the US for transplant eligible MM but no large prospective randomized comparisons of these exist. **Methods:** We analyzed outcomes of 851 US and Canadian pts transplanted within 24 mo of diagnosis after first line therapy with the doublets RD (228) or VD (202) or the triplets CVD (102) or RVD (319) using prospectively reported data to the CIBMTR. **Results:** Doublet use declined over time with majority (63%) receiving RVD or CVD after 2010. Median number of cycles were 4 and median time to transplant was 6-7 mo with 90% transplanted within 12 mo of diagnosis. Disease stage, co-morbidity index, cytogenetic risks were similar between cohorts. Pts with renal dysfunction were more likely to receive CVD. Overall induction response was 94%. VGPR or better responses pre-AHCT were superior for RVD (56%) vs. CVD (46%) or doublets (44%). All patients received 200 mg/m2 Melphalan for single AHCT. Median follow up was 36 months. Use of R or V maintenance was higher in triplet cohorts (79% in RVD, 78% in CVD and 54% in doublets). Post AHCT responses, PFS/OS are in table. PFS from diagnosis was superior for RVD (@3yrs 63% vs. 50% in CVD and 52% in RD/VD, p=0.04). Non-relapse mortality was similar across cohorts while relapse was higher with doublets (@ 2 years 30% for RVD vs. 37% for CVD vs. 41% for RD/VD, p=0.01). In multivariate analysis, relapse risk was higher for doublets and high risk cytogenetics. PFS was inferior with doublets, adverse cytogenetics, and <VGPR response pretransplant. Adverse cytogenetics and ISS III were associated with worse OS while induction was not. **Conclusions:** While no survival differences were seen, triplet induction led to deeper post-AHCT responses, lower relapse and higher PFS. The latter could be confounded by higher use of maintenance with triplets. At 3 years follow up, RVD induction appears superior to both CVD and doublets.

Day 100 MM response	CVD	RVD	VD/RD
sCR/nCR	11%	11% 5%	
CR	19%	26%	26%
VGPR	31%	29%	32%
PR	27%	22%	24%
SD	11%	10%	9%
PROGRESSION	<1%	2%	3%
PFS and OS from transplant	CVD	RVD	VD/RD
3 yr PFS (p=0.01)	39 (25-53)%	59 (52-66)%	44 (39-49)%
3 yr OS (p=0.60)	68 (52-80)%	83 (78-89)%	84 (80-88)%
PFS and OS from start of induction			
3 yr PFS (p=0.04)	50 (37-63)%	63 (57-70)%	52 (46-57)%
3 yr OS (p=0.47)	80 (68-89)%	88 (83-93)%	88 (84-91)%



BP-014

Myeloma Canada Research Network (MCRN) 001 Trial with Intravenous (IV) Busulfan + Melphalan (BuMel) as Enhanced Conditioning, followed by Lenalidomide (Len) Maintenance in Newly Diagnosed Multiple Myeloma (MM) Patients (Pts): First Results of Minimal Residual Disease (MRD) and Hevylite(TM) Chain (HLC) Assays at Day 100 Post Autologous Stem Cell Transplant (ASCT)

D. Reece,[1] G.P. Rodriguez,[1] M. Pantoja,[1] H. Paul,[1] C.P. Venner,[2] D. White,[3] J. Stakiw,[4] M. Sebag,[5] T. Comeau,[6] K. Song,[7] J. Roy,[8] L. Minuk,[9] J. Tay,[10] V. Kukreti,[1] S. Trudel,[1] C. Chen,[1] R. Tiedemann,[1] A. Prica[1]

[1]Department of Medical Oncology and Hematology, Princess Margaret Cancer Centre, Toronto, ON, Canada; [2]Cross Cancer Institute,

Table 1 Comparison of Response Rates by Conventional Serum/Urine Parameters and Marrow Flow Cytometry for MRD after Induction Chemotherapy and at Day 100 Post-ASCT

# of Conventional Ig Responses and MRD Negativity														
	# Evalu-able	Total # MRD negative (%)	CR		VGPR		PR		MR		SD			NA
			Total	MRD(-)	Total	MRD (-)	Total	MRD (-)	Total	MRD (-)	Tota	MRD(-)	Total	MRD(-)
After btz-based induction	63	17 (27%)	5	4	23	8	29	5	4	0	1	0	1	1
Day 100 post-ASCT	49	15 (30%)	8	4	26	11	14	0	1	0	0	0	0	0

Abbreviations: Bu = Busulfan; Mel = Melphalan; ASCT = autologous stem cell transplantation; btz = bortezomib; CR = complete remission; Ig = immunoglobulin; MR = minimal response; SD = Stable Disease; MRD = minimal residual disease; PR= partial remission; VGPR= very good PR; NA = Not Available

Edmonton, AB, Canada; [3]Queen Elizabeth II Health Sciences Centre, Halifax, NS, Canada; [4]Saskatoon Cancer Center, Saskatoon, SK, Canada; [5]McGill University Health Centre, Montreal, QC, Canada; [6]Saint John Regional Hospital, St. John, NB, Canada; [7]Vancouver General Hospital, British Columbia Cancer Agency and University of British Columbia, Leukemia/Bone Marrow Transplant Program of British Columbia, Vancouver, BC, Canada; [8]Division of Hematology and Oncology, Maisonneuve-Rosemont Hospital, Montreal, QC, Canada; [9]London Health Sciences Centre, London, ON, Canada; [10]The Ottawa Hospital, Ottawa, ON, Canada

Background: The use of conventional immunoglobulin (Ig) markers to define MM responses has many limitations and better tests are required to determine disease status. We utilized both, serial bone marrow MRD detection by multiparameter flow cytometry (MFC) and serial HLC assays to monitor evidence of myeloma throughout the current study. **Methods:** Pts eligible for ASCT, who received btz-based induction therapy (usually CyBorD), in the absence of disease progression (PD), were enrolled in this phase 2 trial in 10 major transplant centers in Canada.

Pts received IV BuMel conditioning, followed by ASCT on day 0. On day 100 post-ASCT, Len 10 mg/day was commenced, escalated to 15 mg/day after 3 cycles if appropriate, and continued until PD. MRD analysis by 8-color MFC and serum HLC were performed before any therapy, prior to ASCT, on day 100 post-ASCT, every 3 mos for the 1st year and every 6 mos thereafter until PD. Between 03/2013 - 05/2015, 117 untreated bone marrow aspirate samples were analyzed for MRD; only 4 samples (3%) were unsatisfactory. In all, 42 (36%) pts either did not meet criteria for enrollment for protocol ASCT or opted for standard conditioning. 66 of a target of 78 pts have undergone ASCT; 65 are evaluable. **Results:** Median age is 57 (34-69); 64.6% are male. Median serum 2-microglobulin is 3.44 mg/L (1.5-20) and albumin 37 g/L (2.8-48.1); 29 pts have ISS stage I; 18 stage II; 13 stage III and 5 are missing data. Ig subtype includes IgG (29), IgG (12), IgA (8), IgA (9), (5), (1) and no data (1). There have been no ASCT-related deaths, and 4 pts have progressed (median F/U 15.8 mos). The best conventional Ig response post-induction in 62 pts is CR in 5 (8%), VGPR in 23 (37%), PR in 29 (47%), MR in 4 (6%) and SD in 1 (2%). In the 49 pts who have reached day 100 post-ASCT, the Ig response is CR in 8 (16%), VGPR in 26 (53%), PR in 14 (29%) and MR in 1 (2%). Tables 1-2 summarize MRD and HLC results at Day 100.

Conclusions:

1) IV BuMel + ASCT and Len maintenance is well tolerated with no deaths to date; 2) at Day 100, 30% of evaluable pts were MRD (-), all of whom were in ≥VGPR by conventional parameters; 3) at Day 100, the strongest correlation between MRD and HLC status was observed in MRD (-) pts, of whom 88.2% had normalized their involved HLC ratios; 4) further F/U is required to determine the long term outcomes, the dynamics and prognosis of MRD negativity, and relationships between MRD status and involved HLC ratio.

Table 2 Comparison of Response Rates by Marrow Flow Cytometry for MRD and Serum Hevylite Assay of the Involved Monoclonal Protein after Induction Chemotherapy and at Day 100 Post-ASCT

	# Evalu-able	MRD negative			MRD Positive		
		Total	Hevylite normal	Hevylite abnormal	Total	Hevylite normal	Hevylite abnormal
After btz-based induction	63	17	15 (88.2%)	1 (5.9%)	41	20 (50%)	12 (29%)
Day 100 post-ASCT	49	15	13 (86.7%)	0	30	17 (56.7%)	9 (30%)

Note: Light chain only patients and those in whom HLC ratios could not be calculated were excluded Abbreviations: Bu = Busulfan; Mel = Melphalan; ASCT = autologous stem cell transplantation; btz = bortezomib; MRD = minimal residual disease