First Report of the Myeloma Canada Research Network (MCRN)-001 Trial Utilizing Bortezomib-Based Induction, Enhanced Conditioning with IV Busulfan + Melphalan (BuMel) and Lenalidomide Maintenance: Feasibility of a National Canadian Study Based on Achievement of Minimal Residual Disease (MRD) Negativity

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Article | Info & Metrics

Abstract

Conventional immunoglobulin (Ig) markers have been used to define multiple myeloma (MM) responses, but assessment of marrow for minimal residual disease (MRD) may provide better information on disease status/prognosis (Paiva B, et al. *Blood* 2008; 112: 4017). We therefore initiated a national multi-center ASCT trial with the goal of producing a high rate of MRD-negativity by using bortezomib (btz)-based induction, enhancing the conditioning regimen and utilizing post-ASCT maintenance.

This phase 2 open label-trial was conducted in 10 Canadian centers. After btz-based induction (usually CyBorD) in the absence of disease progression, patients (pts) received BuMel conditioning (IV busulfan 3.2 mg/kg days -5 to -3 or days -6 to -4 + melphalan 140 mg/m^2 day -2 or day -3), followed by ASCT on day 0. On day 100 post-ASCT, lenalidomide (len) 10 mg/day was commenced, escalated to 15 mg/day after 3 cycles if appropriate, and continued until disease progression.

Bone marrow aspirate (BMA) samples were shipped centrally for MRD analysis by 15-color multiparameter flow cytometry (MFC) before any therapy, prior to ASCT, on day 100 post-ASCT, every 3 mos for the 1st year and every 6 mos thereafter until progression.

Between 03/2013 - 07/2014, 99 newly diagnosed MM pts provided untreated BMA samples for MRD analysis. To date, 42 of a planned target of 78 pts have completed induction therapy have undergone ASCT and 39 are evaluable so far. 25 of the 99 (25%) who provided initial marrow samples did not meet criteria for enrollment: 3 (3%) had poor BMA samples; 3 (3%) did not have confirmed MM; 6 (6%) did not proceed with ASCT (1 due to progression); 1 (1%) had received dexamethasone prior to MRD analysis; 1 (1%) died during induction and 11 (11%) withdrew consent/opted for standard conditioning.

Median age of the 39 evaluable pts is 53 (39-67); 64% are male. Median serum β2-microglobulin level is 3.64 mg/L (1.7-2(albumin 37 g/L (2.8-48.1); 17 pts have ISS stage I; 9 have stage II; 9 have stage III MM and 4 have missing data. Ig subtype includes IgGκ in 16 (40%), IgGλ in 4 (10%), IgAκ in 5 (13%), IgAλ in 8 (21%), IgMλ in 1 (3%), κ in 1 (3%); non-secretory in 2 (5%) and no data in 2 pts (5%).

Post-ASCT, only 4 SAEs have occurred: atrial fibrillation (2), acute kidney injury (1) and sepsis (1). There have been no ASCT related deaths, and no pt has progressed at a median follow-up of 7.8 mos (range: 4.8-10.1).

The best Ig response post-induction in the 31 pts with available restaging data is CR in 5 (16%), VGPR in 9 (29%), PR in 13 and SD in 1 (3%). 27 pts have reached day 100 post-ASCT and 8 pts have been formally evaluated. In these 8, the Ig response is CR

in 2 (25%), VGPR in 5 (63%) and PR in 1 (12%). Table 1 summarizes MRD results to date.

			# Conventional Ig Responses [# MRD negative]			
Time point of assessment	# Evaluable	Total # MRD negative	CR	VGPR	PR	MR
After btz-based induction	31	6	5 [3]	9 [1]	13 [2]	0
Day 100 post-ASCT	8	2	2 [2]	5[0]	1[0]	0
During len maintenance	5	1	0	5 [1]	0	0

Table 1.

Comparison of conventional Ig response rates and achievement of MRD negativity

Conclusions: 1) MFC performed on pre-therapy marrow samples to allow subsequent evaluation for MRD was successful in 97% of pts using a central lab; 2) IV BuMel was well-tolerated with few SAEs and no ASCT-related deaths; 3) MRD and conventional Ig responses may not correlate well; 4) Further F/U is required to determine the dynamics of MRD achievement and long term outcomes with this approach.

Disclosures Reece: *Novartis:* Honoraria, Research Funding; *BMS:* Research Funding; *Merck:* Research Funding; *Millennium:* Honoraria, Research Funding; *Janssen:* Consultancy, Honoraria, Research Funding; *Celgene:* Consultancy, Honoraria, Research Funding; *Otsuka:* Honoraria, Research Funding; *Amgen:* Honoraria. **Off Label Use**: Lenalidomide maintenance after ASCT. **Venner**: *Celgene:* Honoraria, Research Funding; *Janssen:* Honoraria. **White**: *Janssen:* Consultancy, Honoraria; *Celgene:* Consultancy, Honoraria. **Sebag**: *Novartis:* Honoraria; *Janssen:* Honoraria; *Celgene:* Honoraria. **Song**: *Celgene:* Honoraria; *Otsuka:* Honoraria; *janssen:* Honoraria. **Tay**: *Celgene:* Honoraria; *Janssen:* Honoraria. **Kukreti**: *Celgene:* Honoraria. **Trudel**: *Glaxo Smith Kline:* Honoraria, Research Funding; *Novartis:* Honoraria; *Celgene:* Honoraria; *Oncoethix:* Research Funding. **Tiedemann**: *Celgene:* Honoraria; *Janssen:* Honoraria. **Chen**: *Millennium:* Research Funding; *Janssen:* Honoraria; *Celgene:* Honoraria, Research Funding

- * Asterisk with author names denotes non-ASH members.

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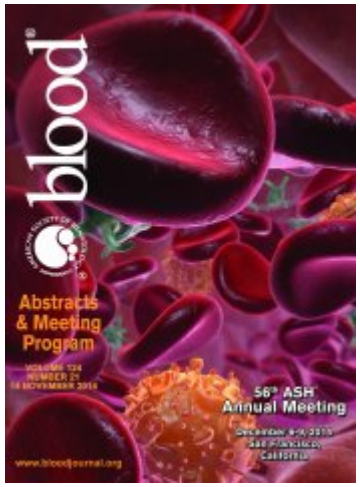

Table of Contents
Volume: 124
Issue: 21
Pages: 3990
DOI: https://doi.org/

Jump to

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