Dose Adjusted Melphalan Yields Comparable MRD-negativity To Full Dose Melphalan In Multiple Myeloma Patients Undergoing Autologous Stem Cell Transplant

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BACKGROUND

Multiple Myeloma (MM) remains an incurable disease. Autologous stem cell transplantation (ASCT) is a standard treatment for eligible patients, with high-dose melphalan (MEL200) as the preferred conditioning regimen. Reduced-dose melphalan (MEL140) is used for older or less fit patients. However, this was not prospectively studied and there has been ongoing debate about the efficacy of reduced dosing.

Minimal residual disease (MRD) is an acceptable surrogate for PFS in MM. This study aimed to investigate the impact of melphalan dose on MRD negativity rates in MM patients undergoing upfront ASCT.

METHOD

We conducted a retrospective, single-center study involving patients with MM who underwent ASCT between 2018 and 2022 at UH Seidman Cancer Center, Cleveland, OH.

129 patients underwent ASCT during that period, 78 of them were planned to get MRD testing, 73 patients were tested at least once and 48 were tested more than once.

MRD testing was performed during the first year from ASCT using the ClonoSEQ next generation sequencing platform.

Median follow up time was 37 months.

RESULTS

Table 1. Baseline Characteristics

Baseline Characteristic	MEL 140 N = 28	MEL200 N = 46	P-value
Age	70.35 (4.25)	59.81 (7.00)	<0.001
Sex (F)	10(36%)	18(39%)	0.8
Race			0.7
Black	4(14%)	8(17%)	
White	24(86%)	36(78%)	
BMI	29.38 (5.66)	31.80 (7.28)	0.13
GFR (>60)	21(75%)	40(87%)	0.3
KPS (>80)	23 (82%)	45 (98%)	0.079
HCT-CI	2.36 (2.28)	1.98 (1.72)	0.7
ISS Stage			0.6
1	6(35%)	5(19%)	
2	7(41%)	13(50%)	
3	4(24%)	8(31%)	
Cytogenetics Risk			0.6
High Risk	11(44%)	14(38%)	
Standard Risk	14(56%)	23(62%)	
Prior Lines of treatment			0.7
1	16(57%)	31(67%)	
2-3	12(43%)	15(33%)	
Induction Regimen			0.1
VRD	22(79%)	32(70%)	
Other triplets	4(14.6%)	5(11%)	
Doublets	1(3.6%)	2(4.4%)	
Quadruplets	1(3.6%)	7(15.2%)	
Status At Transplant			0.7
CR	6(21%)	14(30%)	
VGPR	19(68%)	27(59%)	
PR	3(11%)	5(11%)	
CD34 infused x10^6/kg	6.05 (3.73)	5.19 (2.48)	0.7

Table 2. Safety Outcomes

	MEL 140 N = 28	MEL200 N = 46	P-value
Time to engraftment (d)	11.36 (0.99)	11.43 (0.81)	0.7
Hospital Stay (d)	15.07 (2.14)	15.61 (5.51)	0.3
Readmissions	4(14%)	10(22%)	0.4
Infection rate	4(14%)	9(20%)	0.8

Figure 1. Rate of MRD negativity based on Melphalan dose

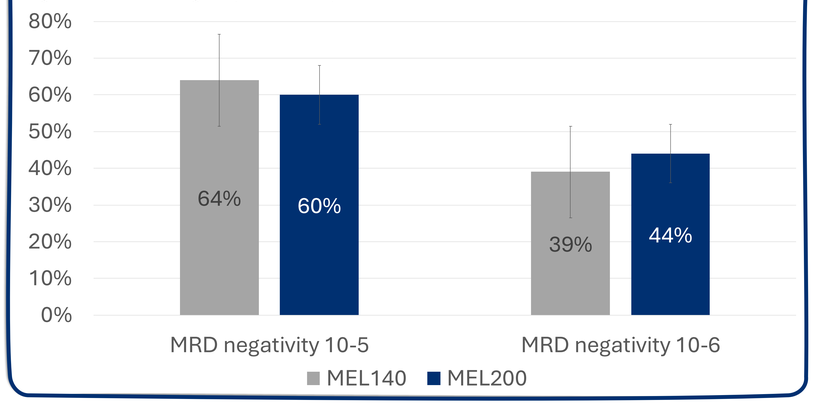


Figure 2. MRD status overtime after ASCT

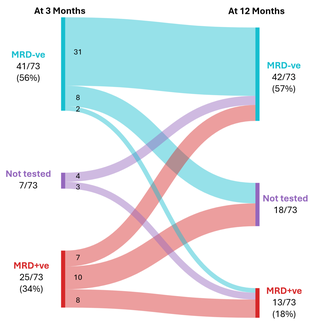


Figure 3. Rate of sustain MRD negativity based on Melphalan dose

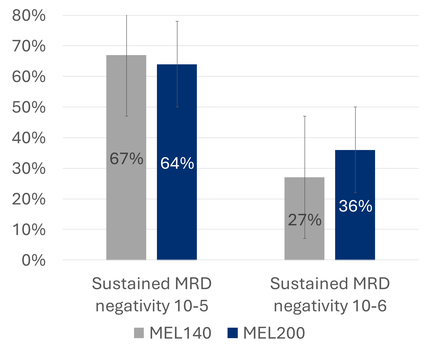
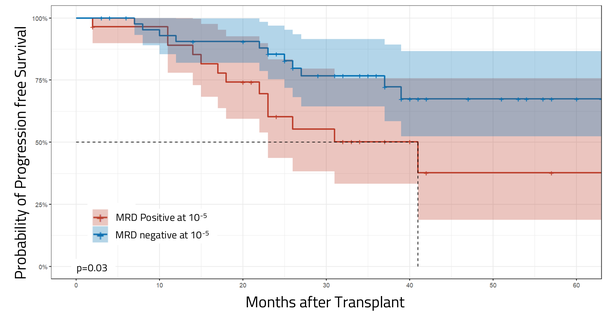
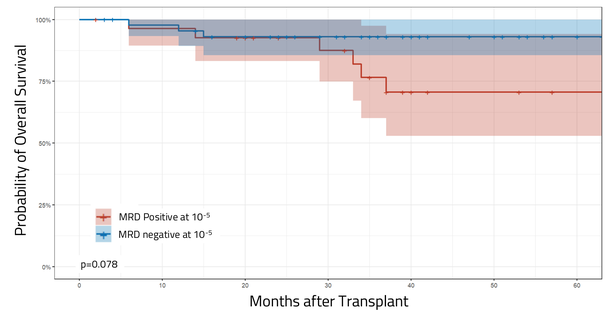


Figure 4. Progression free and Overall survival for patients with MM based on MRD status





Supplementary data:

		MRD negativity (10^{-5})				MRD negativity (10^{-6})			
	N	TOTAL	MEL140	MEL200	P-value	TOTAL	MEL140	MEL200	P-value
Intention-to-treat									
MRD-negative status, n (%)	129	45 (35%)	18(41%)	27(32%)	0.3	31(24%)	11(25%)	20(24%)	0.9
≥12 mo sustained	129	31 (24%)	10(23%)	21(25%)	0.8	16(12%)	4(9%)	12(14%)	0.4
Tested									
MRD-negative status, n (%)	73	45 (62%)	18(64%)	27(60%)	0.7	31(42%)	11(39%)	20(44%)	0.7
≥12 mo sustained	48	31(65%)	10(67%)	21(64%)	0.8	16(33%)	4(27%)	12(36%)	0.5

CONCLUSIONS

Our real-world analysis demonstrates that MEL140 yields similar deep post-transplant remissions as MEL200, translating to improved PFS for patients achieving MRD negativity, regardless of the dose used.

CONTACT INFORMATION

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