Rates of Upfront Autologous Stem Cell Transplantation (ASCT) in Newly Diagnosed Multiple Myeloma (NDMM): An updated report from the MRDR

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EBMT European Society for Blood and Marrow Transplantation

Background

Despite clear evidence from both clinical trial and real world patient populations for the use of autologous stem cell transplantation (ASCT) as part of front-line therapy in newly diagnosed multiple myeloma (NDMM), utilisation rates are still lower than expected.[1-3] ASCT rates in patients considered age eligible have recently been reported as 43%, 55%, and 59% in published literature in the U.K., Australia, and the U.S. respectively.[1-3] In Australia and New Zealand patients are generally considered eligible for ASCT if they:[1]

- are <75 years
- have a good performance status
- have no significant comorbidities/frailty

However, the biological fitness for ASCT is ultimately at the discretion of the treating physician.

Methods

We conducted a retrospective review of adult patients registered on the Myeloma and Related Disease Registry (MRDR), a prospectively maintained database from 23 sites across Australia (20) and New Zealand (3). Patients aged ≤70 with NDMM from June, 2012 to Oct, 2016 with review data available at least 12 months post diagnosis were eligible for analysis. Baseline characteristics, therapies and outcomes were compared between recipients and non-recipients using chi square tests for categorical variables and rank sum tests for continuous variables. Kaplan Meier survival analysis was used to estimate time to disease progression and overall survival.

Results

- **364 of 489 patients received an ASCT (74.4%)- see table 1**

Baseline characteristics, disease response to induction therapy and treatment are shown in tables 2 and 3

- **Median time from diagnosis to first therapy was the same in both the ASCT and non-ASCT group (21 days)**
- **Median time to ASCT was 200.5 days.**

Table 1: ASCT utilisation rates by age group

Patient Age (years)	All Patients	<50	50-55	55-60	60-65	65-70	p-value
N	489	70	64	94	123	138	
ASCT	364 (74.4%)	61 (87.1%)	54 (84.4%)	75 (79.8%)	97 (78.9%)	77 (55.8%)	<0.001

Table 2: Baseline Characteristics (All patients)

Baseline Characteristics	Non-ASCT (n=125)	ASCT (n= 364)	p-value
Median Age at Diagnosis (years, IQR)	64.7 (58.0-67.9)	59.6 (52.9, 64.2)	<0.001
Male (%)	71 (56.8%)	233 (64.0%)	0.15
ISS			0.005
1	15 (18.5%)	100 (37.7%)	
2	38 (46.9%)	101 (38.1%)	
3	28 (34.6%)	64 (24.2%)	
R-ISS 3	12 (21.1%)	19 (10.9%)	0.051
ECOG ≥2	19 (24.4%)	40 (15.6%)	0.077
LDH (U/L, median, IQR)	204 (168,261)	179.5 (146-229)	0.018
Cr (µmol/L, median, IQR)	91 (70, 134)	82 (68, 99)	0.013
eGFR, mL/min/1.73 m² median (IQR)	69 (43, 81)	80 (65, 90)	<0.001
Bone Lesions	61 (48.8%)	232 (63.7)	0.003

Table 3: Therapy and Response Characteristics (All patients)

	Non-ASCT (n= 125)	ASCT (n=364)	p-value
Induction Therapy			
Bortezomib-based	99 (86%)	341 (94.2%)	
Thalidomide-based	8 (7.0%)	8 (2.2%)	
Bortezomib+ thalidomide	4 (3.4)	7 (1.9%)	
Other	4 (3.5%)	6 (1.7%)	
			<0.001
Days to therapy from diagnosis	21 (10-39)	21 (9, 45)	0.49
Cycles of bortezomib based therapy, median (IQR)	4 (4, 4)	6 (4, 9)	<0.001
Disease Response to Induction Therapy			
≥PR	81 (77.9%)	294 (89.9%)	0.001

Patients who did not receive an ASCT were:

- **Older (median age 64.7 vs 59.6 years, p<0.001)**
- **Had poorer renal function (eGFR 69 vs 80 (p<0.001), Cr (91 vs 82 (p=0.013)) and higher ISS (p=0.005)**
- **Of patients with known data:**
  - **ISS stage predicted for ASCT utilisation (ISS 3 34.6% vs 24.2% in the non-ASCT vs ASCT groups respectively**
  - **Neither higher ECOG (≥2) or higher R-ISS (R-ISS 3) reached statistical significance for prediction of patients not receiving an ASCT (ECOG ≥2 24.4% vs 15.6%, p=0.077 and R-ISS 3 21% vs 10.9%, 0.051) in the non-ASCT versus ASCT groups respectively**
  - **Patients not receiving an ASCT were less likely to have been treated with bortezomib-containing induction (86% vs 94.2%, see table 3)**
- **Patients who did not receive an ASCT had a shorter progression free survival (PFS) (median 25.3 vs 33.5 months, p<0.001).**
- **Thalidomide-containing therapy was most frequently used for post ASCT maintenance (72%).**

Contacts and Acknowledgments

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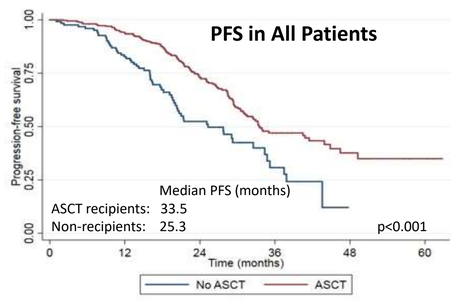
When patients were compared based on age group (<65 years vs patients 65-70 years)

- **ASCT utilisation rates were higher in younger patients (82% in patients <65 years vs 55.8% in patients >65 years) see table 4**
- **Younger patients receiving an ASCT had an improved OS compared to older patients (68.2 months vs 60.9 months). However, ASCT recipients in both groups had a longer median OS than non-recipients (Median OS 68.2m vs 37.4m in patients <65y and 60.9m vs 43.1 in patients 65-70y in ASCT recipients and non-recipients respectively, see table 5) suggesting that ASCT is a beneficial therapy even in older patients.**
- **ASCT recipients had an improved progression-free survival (PFS) compared with non-recipients in the whole cohort (median PFS 33.5m (30.9-43.9) vs 25.4m (20.1-34.4) p<0.001) and this PFS benefit was still seen in older (65-70y) patients (median PFS 32.4 (29.4m-NR) vs 20.7 (17.6m-29.1m) p<0.001) in ASCT recipients and non-recipients respectively**

Baseline characteristics and outcomes of these two groups are shown in tables 4 and 5 respectively.

Table 4: Baseline Characteristics, response, induction therapy by age group

	Patients aged <65 years			Patients aged 65-70 years		
	No ASCT (n=64)	ASCT (n=287)	p value	No ASCT (n=61)	ASCT (n=77)	p value
ECOG ≥2	25.6%	10.8%	0.18	15% (3/20)	8% (2/25)	0.46
Bone lesions	43.8%	64.1%	0.003	54.1%	62.3%	0.33
Cr	90 (66-226)	79 (68-91)	0.04	79.5 (69-108)	84.5 (67-103.5)	0.95
eGFR	75 (27-90)	87 (69-90)	0.02	69 (60-90)	79 (60-90)	0.3
Days to therapy from diagnosis	20 (8.5, 38)	21 (11, 41)	0.68	23 (13, 47)	19.5 (6, 34)	0.058
Cycles of bortezomib based therapy, median (IQR)	5 (4, 8)	4 (4, 4)	<0.001	8 94, 9)	4 (3, 4)	<0.001
Response ≥PR	75.5%	88.8%	0.012	88%	94.1%	0.017



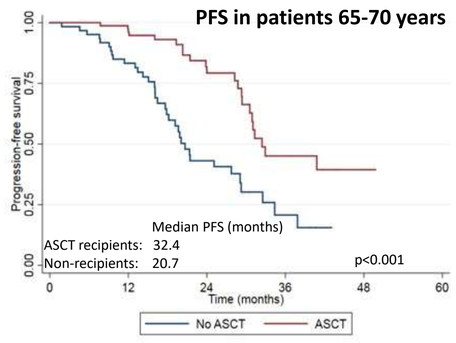
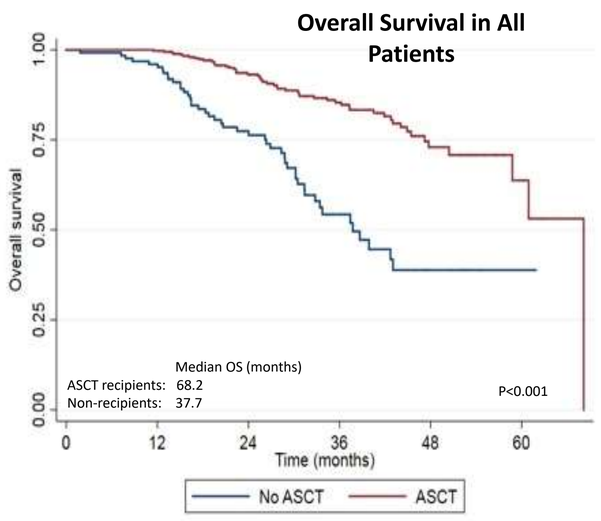
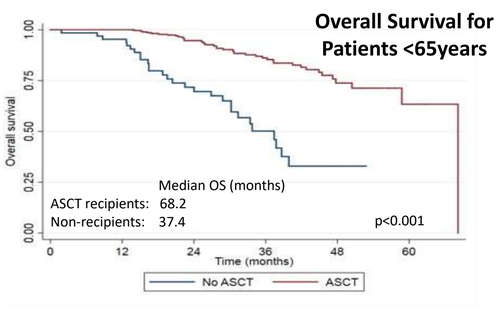
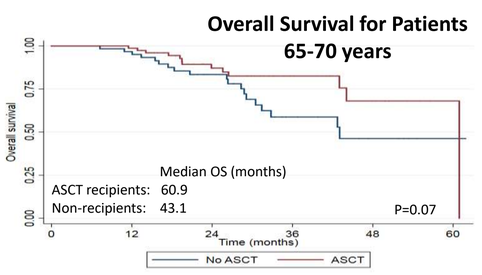


Table 5: Overall Survival by age group

	All Patients		<65 years		65-70 years	
	No ASCT n=125	ASCT n=364	No ASCT (n=64)	ASCT (n=287)	No ASCT (n=61)	ASCT (n=77)
Median OS in months (95% CI)	37.7 (31.4, NR)	68.2 (58.8, NR)	37.4 (30.2-39.9)	68.2 (58.8, NR)	43.1 (30.5, NR)	60.9 (44.1, NR)







Conclusions

- **ASCT is a highly effective therapy in MM but currently appears under-utilised in Australia/New Zealand.**
- **Further study to elucidate the reasons for this under-utilisation is indicated.**
- **Renal function and ISS stage at diagnosis appeared to be used as a guide to patient fitness for ASCT in this cohort while statistically ECOG status did not.**
- **Disease response to therapy (≥PR) was predictive of physician decision to undertake ASCT in all patients**
- **ASCT is utilised less frequently in older patients and not receiving an ASCT is associated with a poorer PFS and OS.**
  - **56% of patients >65-70 years received an ASCT compared to 82% of patients <65 years (p<0.001).**
- **Consideration of an ASCT may benefit patients in this group**
  - **Further study with larger cohorts of patients are required to confirm if a true benefit of ASCT exists in patients >65 years**

References

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