

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

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Background: Despite clear evidence from both clinical trial and real world patient populations for the use of 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/New Zealand patients are considered generally eligible for ASCT are:⁴

- <75 years
- Have a good performance status
- No significant comorbidities/frailty

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

Method: We conducted a retrospective review of adult patients registered on the Myeloma and Related Disease Registry (MRDR), a prospectively maintained database from 25 sites across Australia (22) and New Zealand (3). Patients aged ≤70 with NDMM from June, 2012 to June, 2015 with at least 12 months completed follow up were included in the analysis (n=218). Baseline characteristics, therapies and outcomes were compared between recipients and non-recipients using appropriate tests. Survival analysis was used to estimate time to disease progression.

Results: Baseline characteristics and therapies are shown in tables 1 and 2.

- 163 of 218 patients received an ASCT (75%).
 - Patients were almost exclusively from major tertiary centres
 - Median time to ASCT was 197 days.
- Patients who did not receive an ASCT were:
- Older (median age 66.1 vs 58.0 years, p<0.0001)
 - Had a lower eGFR 71.5 vs 86.5 (p=0.004) but not higher Cr (86 vs 79 (p=0.11)) or higher ISS
 - However they had a similar time from diagnosis to therapy (19 vs 20 days)
 - Of patients with known data:
 - Neither higher ECOG (≥2) or ISS stage 3 predicted for patients receiving an ASCT (Higher ECOG 19.4% vs 9.7%, p=0.12 and ISS 3 32.5% vs 22.9%, p=0.22 in the non-ASCT and ASCT group respectively).

- Patients not receiving an ASCT were less likely to have been treated with bortezomib-based induction (88.0% vs 93.9%, p=0.046) but more likely to be treated with melphalan or thalidomide-containing induction (8.0% vs 0%, p<0.001 and 8.0% vs 3.7%, p=0.21 respectively).

Table 1: Baseline Characteristics

| Baseline Characteristics | ASCT (n=163) | Non-ASCT (n= 55) | p-value |
|---------------------------------|------------------|------------------|---------|
| Median Age at Diagnosis (years) | 58.0 (21.6-69.6) | 66.1 (35.5-70.0) | <0.001 |
| Male (%) | 100 (61%) | 29 (52.9%) | 0.26 |
| ISS | | | |
| 1 | 53 (32.5%) | 11 (20.0%) | |
| 2 | 48 (29.4%) | 16 (29.1%) | |
| 3 | 30 (18.4%) | 13 (23.6%) | |
| Unknown | 32 (19.6%) | 15 (27.3%) | 0.27 |
| ECOG | | | |
| 0 | 49 (30.1%) | 12 (21.9%) | |
| 1 | 53 (32.5%) | 17 (30.9%) | |
| 2 | 9 (5.5%) | 3 (5.5%) | |
| 3 | 2 (1.2%) | 4 (7.4%) | |
| Unknown | 50 (30.7%) | 19 (34.5%) | 0.86 |
| LDH | 173 (132-226) | 183 (159-254) | 0.79 |
| Cr | 79 (67-96) | 86 (69-113) | 0.11 |
| eGFR | 86.5 (66.5-90) | 71.5 (57-90) | 0.004 |
| Bone Lesions | 67.4% (110/163) | 52.7% (29/55) | 0.049 |

Table 2: Therapy Characteristics

| | ASCT (n=163) | Non-ASCT (n= 55) | p-value |
|----------------------|--------------|------------------|---------|
| Bortezomib-based | 153 (93.9%) | 44 (88.0%) | 0.046 |
| Thalidomide-based | 6 (3.7%) | 4 (7.3%) | 0.21 |
| Melphalan containing | 0 (0.0%) | 4 (7.3%) | <0.001 |
| Other | 2 (1.2%) | 2 (3.6%) | |
| Unknown | 0 (0.0%) | 5 (9.1%) | |
| Maintenance Therapy | 105 (64.4%) | | |

- Patients who did not receive an ASCT had a shorter progression free survival (PFS) (median 19.4 vs 31.7 months, p<0.001).
 - Maintenance therapy was used in 105 (64%) of patients post ASCT with thalidomide containing therapy most frequent (73%)
- When patients were compared based on age group (≤65 years vs patients >65 years)
- ASCT utilisation rates were higher in younger patients (85% in patients ≤65 years vs 50% in patients >65 years).
 - Younger patients receiving an ASCT had an improved PFS compared to older patients (40.5 months vs 31.09 months) while there was no difference between the two groups in those not receiving an ASCT (20.5 months vs 19.7 months)
 - Baseline characteristics and outcomes of these two groups are shown in tables 3 and 4.

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.
- ECOG did not appear statistically to be used as a guide to patient fitness for ASCT in this cohort.
- ASCT is utilised less frequently in older patients and not receiving an ASCT is associated with a poorer PFS.
- 50% of patients >65-70 years received an ASCT compared to 85% 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

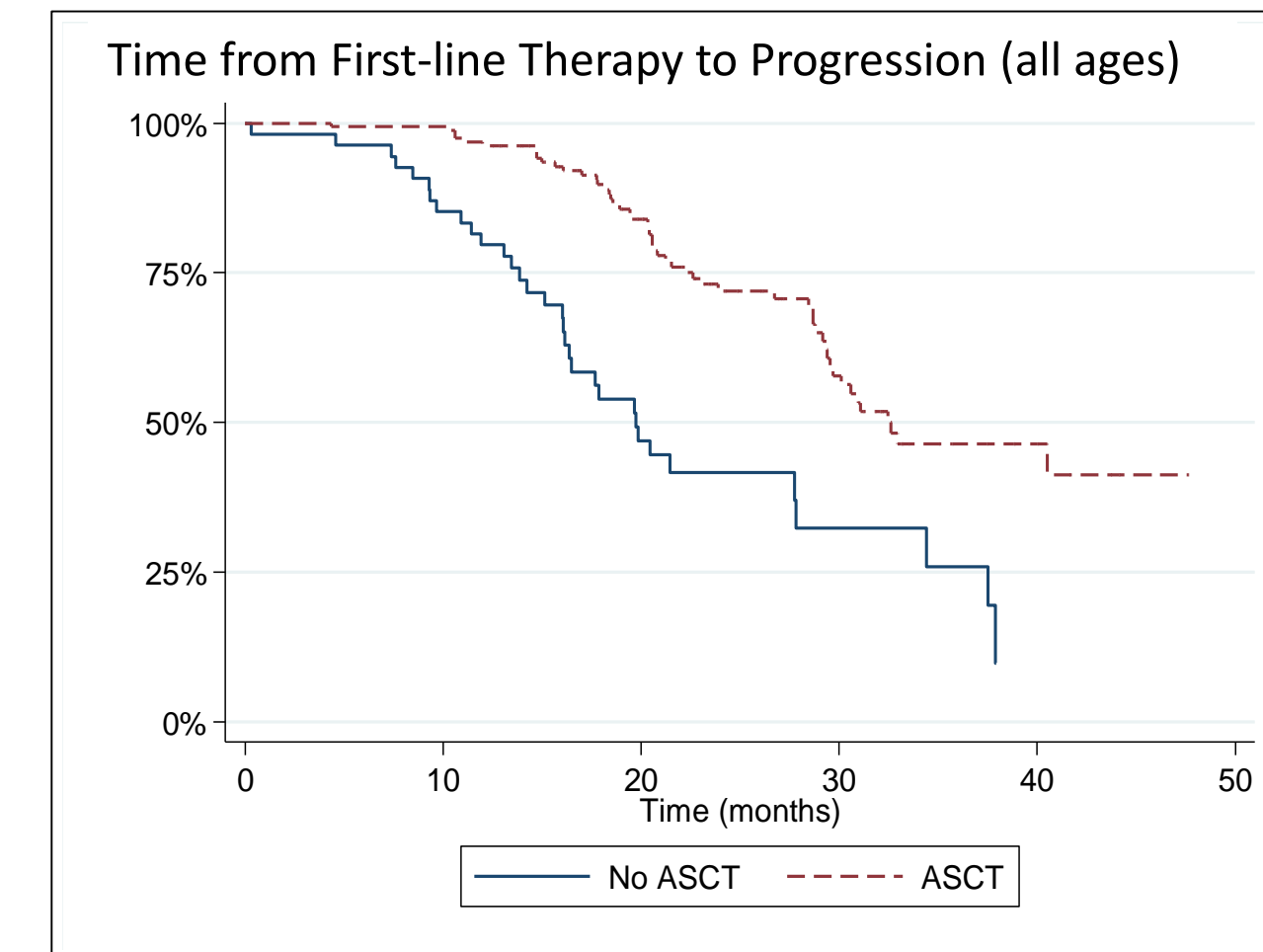


Table 3: Baseline Characteristics by age group

| | Patients aged ≤65 years | | | Patients aged >65-70 years | | |
|---------------------|-------------------------|--------------|---------|----------------------------|-----------------|---------|
| | No ASCT | ASCT | p value | No ASCT | ASCT | p value |
| ECOG ≥2 | 25% (4/16) | 10% (9/88) | 0.1 | 15% (3/20) | 8% (2/25) | 0.46 |
| Bone lesions | 39.1 (9/23) | 67% (88/131) | 0.01 | 62.5% (20/32) | 68.8% (22/32) | 0.6 |
| Renal insufficiency | 21.7% (5/18) | 4.6% (6/131) | 0.003 | 3.1% (1/32) | 12.5% (4/32) | 0.16 |
| Cr | 90 (66-226) | 79 (68-91) | 0.04 | 79.5 (69-108) | 84.5 (67-103.5) | 0.95 |
| eGFR | 87 (69-90) | 87 (69-90) | 0.02 | 69 (60-90) | 79 (60-90) | 0.3 |

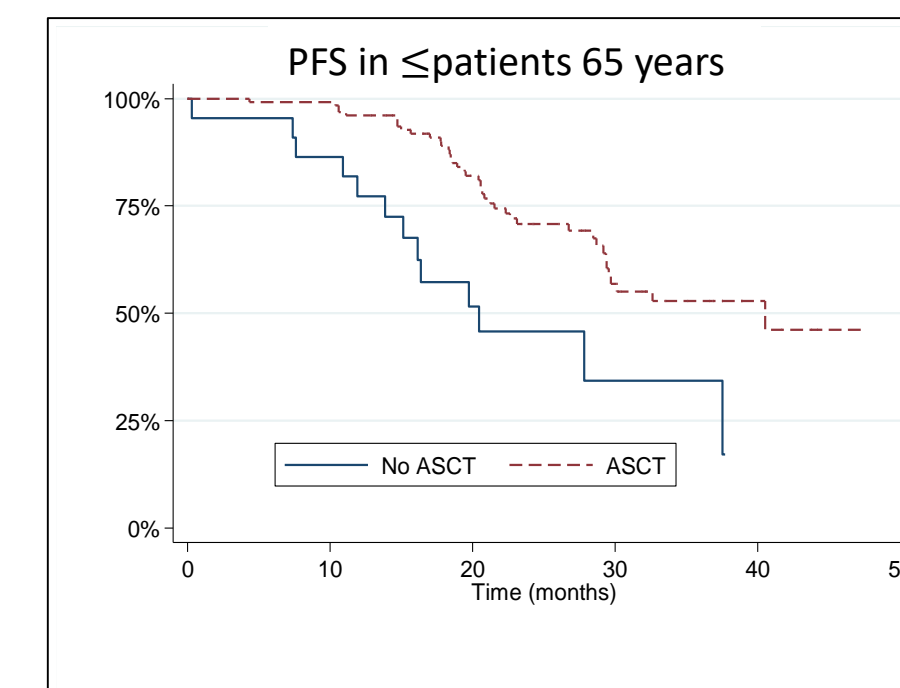
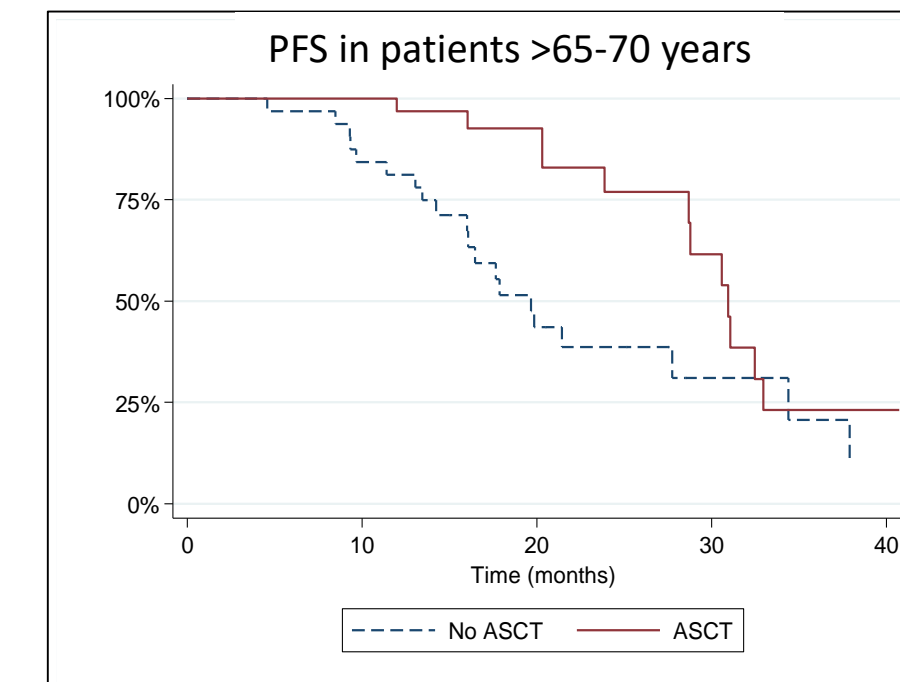


Table 4: PFS by age group

| | ≤65 | | 65-70 | |
|----------------------------|------------------|-----------------|-------------------|--------------------|
| | No ASCT (n=13) | ASCT (n=43) | No ASCT (n=20) | ASCT (n=13) |
| Median PFS in months (IQR) | 20.5 (13.9-37.5) | 40.5 (22.3, NR) | 19.7 (13.4, 34.4) | 31.09 (28.7, 40.9) |

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