Maintenance Therapy but Not Tandem Autologous Stem Cell Transplant (ASCT) Improves outcomes in Multiple Myeloma with High-Risk Cytogenetics: Results from The Canadian Myeloma Research Group (CMRG) Database

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Background: Studies evaluating tandem autologous transplantation for multiple myeloma (MM) show conflicting results. However subgroup analysis suggests that those with high-risk disease may see a modest benefit from tandem transplant. These studies were not powered single versus tandem ASCT in this population, so this question remains unanswered. We used the CMRG database to compare single versus tandem ASCT for myeloma with high-risk cytogenetics.

Methods: The primary objective was to compare PFS in MM patients with high-risk cytogenetics (p53 deletion, t(4;14), t(14;16)) identified from the CMRG database undergoing front-line single or tandem ASCT from 01/2010 to 06/2019. Secondary objectives compared OS, ORR, and outcomes based on whether post-transplant maintenance was given. OS and PFS rates were calculated from the date of first ASCT using the Kaplan-Meier method. ORR was assessed by Chi-square using best response post ASCT.

Results: There were 302 single and 125 tandem transplants, followed by maintenance therapy in 190 (63%) and 96 (77%) respectively. Translocation (4;14) was seen in 209 (49%), t(14:16) in 61 (15.6%) and delP53 in 22 (52%) with more than one abnormality in 65 patients. The most common induction regimen consisted of cyclophosphamide, bortezomib, and steroids, (83%) followed by bortezomib and dexamethasone (8%) and dexamethasone alone (4.7%). Forty-seven patients (11%) required reinduction prior to first ASCT with regimens including RVD (49%), Rd (23%) and others (D/DT/VD-PACE, CyBor-D, KRD, VD, IxaRD, 28%). Maintenance was prescribed to 286 patients with regimens including lenalidomide ± dexamethasone (65%), lenalidomide + proteasome inhibitor ± dexamethasone (22%), proteasome inhibitor ± dexamethasone (11%) and others (2%). Patient characteristics are summarised in table 1.

The overall response rate was 93.9% (94.5% for single ASCT and 92% for tandem ASCT). PFS at 3 years was 41.1% (single) and 45.7% (tandem) with median PFS 26 vs 35 months respectively (p=0.0621). Three year OS was 71.5% (single) and 83.8% (tandem), median OS 82 vs 88 months (p=0.0060). Both PFS and OS were improved with the use of maintenance therapy, regardless of the number of transplants. PFS at 3 years was 52.1% for those receiving maintenance therapy compared to 21.7% for no maintenance (median 42 vs 16months, p<0.0001). Overall survival was 79.5% with maintenance vs 63.6% without (median 92 vs 60 months, p<0.0001).

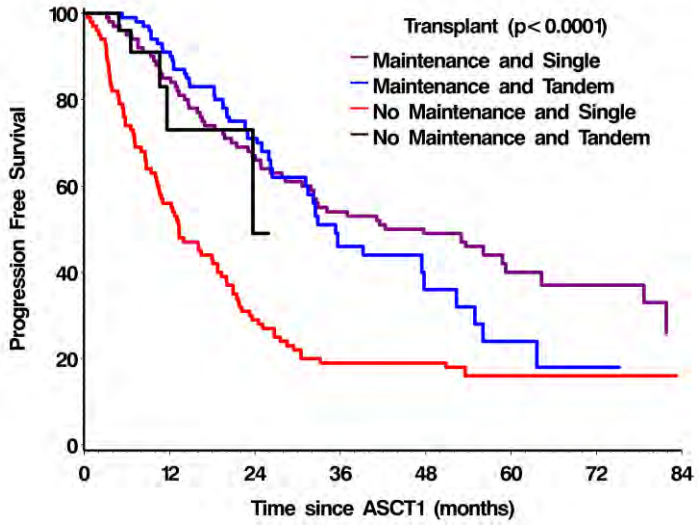
Figures 1 shows PFS and OS for single or tandem transplant, with or without maintenance therapy. There was no difference in PFS or OS after a single or tandem transplant when maintenance was given. PFS for single or tandem ASCT with maintenance at 3 years was 53.7% and 46.3% respectively (p=0.527). Three year OS rates were 76.7% and 85.6% (p=0.0962). However, PFS was better with tandem compared to single ASCT when no maintenance was given. PFS at 3 years for single transplant with no maintenance was 19.0% (median 13 months) vs 48.9% (median 23.7 months) for tandem without maintenance (p=0.0084), while OS were not statistically different (62.4% vs 74.7%, median 60 months vs not reached, p=0.5271).

Conclusions: Tandem ASCT does improve outcomes for MM with high-risk cytogenetics. However, no difference in PFS or OS is seen between single or tandem ASCT when maintenance therapy is used. Tandem ASCT was beneficial in improving PFS when maintenance therapy was not given. These results suggest that, with widespread use of maintenance following ASCT, tandem transplant for high-risk disease is not necessary.

Table 1.

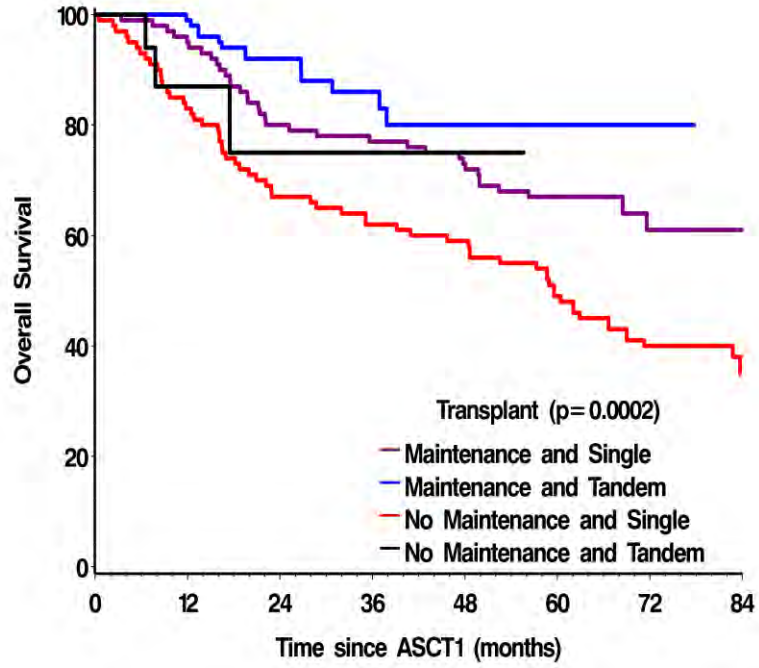
Baseline Characteristic	All ASCT N = 427(%)	Single ASCT N = 302(%)	Tandem ASCT N = 125(%)
Male	260 (61)	178 (59)	82 (66)
t(4;14)			
Positive	209 (48.9)	152 (50.3)	57 (45.6)
Negative	177 (41.4)	128 (42.4)	49 (39.2)
Unknown	41 (9.6)	22 (7.3)	19 (15.2)
t(14;16)			
Positive	61 (14.3)	46(15.2)	15 (12)
Negative	223 (52.2)	176 (58.3)	47 (37.6)
Unknown	143 (33.5)	80(26.5)	63 (50.4)
Del p53			
Positive	222(52.0)	154 (51.0)	68 (54.4)
Negative	165 (38.6)	120(39.7)	45 (36)
Unknown	40 (9.4)	28(9.3)	22 (17.6)
Maintenance			
Yes	286 (67)	190 (62.9)	96 (76.8)
No	141 (33)	112 (37.1)	29 (23.2)
ISS Stage			
I	98 (25.7)	67 (24.5)	31 (28.9)
II	150 (39.4)	112 (40.9	38 (35.5)
II	133 (34.9)	95 (34.7)	38 (35.5)
Missing	46	28	18
IG Type			
IgG	222 (52)	162 (53.6)	60 (48)
IgA	125 (29.3)	85 (28.2)	40 (32)
FLC	79 (18.5)	54 (17.9)	25 (20)
Non-secretory	1 (0.2)	1 (0.3)	0
FLC Type			
Kappa	258 (62.0)	195 (65.9)	63 (52.5)
Lambda	158 (38.0)	101 (34.1)	57 (47.5)

Figure 1. Outcomes for Single and Tandem ASCT with or Without Maintenance
Figure 1a. Progression Free Survival



3 year PFS
53.7%
46.3%
19%
48.9%

Figure 1b. Overall Survival



3-year OS
76.7%
85.6%
62.4%
74.79%