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POSTER ABSTRACTS

731.AUTOLOGOUS TRANSPLANTATION: CLINICAL AND EPIDEMIOLOGICAL

Outcomes of Patients with Multiple Myeloma and 1q Gain/Amplification Receiving Autologous Hematopoietic Stem Cell Transplant: The MD Anderson Cancer Center Experience

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Background: There is contradictory data regarding the prognostic impact of additional copy numbers of chromosome 1q (1q+) on the outcomes of newly diagnosed multiple myeloma (NDMM) patients, and there is scarce data in the context of autologous stem cell transplantation (autoSCT). In this report, we studied outcomes of NDMM patients with 1q+ who received induction with contemporary anti-myeloma agents, followed by autoSCT and post-transplant maintenance therapy.
Methods: We conducted a retrospective single-center chart review analysis of adult NDMM patients with 1q21 gain or amplification (3 or ≥4 copies of 1q, respectively; 1q+) detected by fluorescence in situ hybridization (FISH) that received autoSCT between 2008-2018. Progression-free survival (PFS) and overall survival (OS) were the primary endpoints.
Results: 213 NDMM patients with 1q+ were included in the analysis, with a median age of 62.5 years and 53% were male. Overall, 169 (79%) patients had 1q gain, while 44 (21%) patients had 1q amplification. The most commonly used induction and conditioning regimens were bortezomib, lenalidomide, and dexamethasone (VRD) (41%) and melphalan (77%), respectively (Table 1). At day 100 after autoSCT and at best post-transplant response, 78% and 87% of patients achieved ≥VGPR, 34% and 56% achieved CR, 38% and 50% achieved MRD negative ≥VGPR, respectively. The median PFS and OS for the entire cohort were 35.5 months and 81.4 months, respectively. 1q amplification was associated with inferior PFS compared to 1q gain (HR=2.03, 95% CI 1.36-3.03, p<0.001; Figure 1).
On multivariable assessment (MVA) for PFS, MRD negative >VGPR before autoSCT and at day 100 post-transplant [(HR=0.56, 95% CI 0.36-0.86, p=0.009) and (HR=0.64, 95% CI 0.44-0.94, p=0.022), respectively] were associated with better PFS, whereas 1q amplification was associated with inferior PFS (HR=1.94, 95% CI 1.29-2.92, p=0.001). On MVA for OS, R-ISS stage III (HR=4.08, 95% CI 1.07-15.50, p=0.039) was associated with inferior OS, whereas achieving MRD negative >VGPR at best post-transplant response was associated with superior OS (HR=0.45, 95% CI 0.24-0.85, p=0.014).
Notably, the percentage of cells with 1q+ was not associated with PFS nor with OS, both when evaluated as a continuous variable and when evaluated as a categorical variable using thresholds of either 30% or 50%. The presence of additional high-risk cytogenetic abnormalities did not adversely affect survival outcomes.
Conclusions: Patients with NDMM and 1q+, especially 1q amplification, have poor survival outcomes, despite the use of contemporary induction regimens, upfront autoSCT and post-transplant maintenance. These patients may benefit from novel treatment modalities, such as CAR-T and bispecific antibodies, earlier in their disease course.

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Table 1. Patient characteristics

Measure	All (N=213) n (%)
Gender, n (%)	
Male	113 (53)
Female	100 (47)
Age at autoSCT (years)	
Median (range)	62.5 (34.1 - 79.9)
Race	
White	143 (67)
Black	41 (19)
Hispanic	18 (8)
Asian	7 (3)
NA	4 (2)
Year of autoSCT, n (%)	
2010-2014	59 (28)
2015-2018	154 (72)
R-ISS, n (%)	
I	40 (19)
II	114 (54)
III	22 (10)
Unknown	37 (17)
ISS, n (%)	
I	71 (33)
II	64 (30)
III	54 (25)
Unknown	24 (11)
Induction treatment, n (%)	
KRD	44 (21)
VCD	27 (13)
VD	29 (14)
VRD	88 (41)
Other/unknown	25 (12)
Conditioning regimen, n (%)	
Bu/Mel based	42 (20)
Mel	165 (77)
Other	6 (3)
Response prior to autoSCT, n (%)	
sCR/CR	38 (18)
nCR/VGPR	98 (46)
PR	62 (29)
SD	6 (3)
PD	9 (4)
MRD status prior to autoSCT, n (%)	
Negative	82 (39)
Positive	126 (59)
Not done	5 (2)
Presence of other high-risk cytogenetics, n (%)	
del17	31 (15)
t(4;14)	30 (14)
t(14;16)	13 (6)
Number of additional copies of 1q+, n (%)	
1	169 (79)
2	18 (8)
>2	26 (12)
Proportion of cells with 1q+ (1 additional copy)	
Number of patients	148
Median (range)	0.2 (0.0 - 1.0)
Proportion of cells with 1q+ (2 additional copies)	
Number of patients	17
Median (range)	0.2 (0.0 - 0.9)
Proportion of cells with 1q+ (≥3 additional copies)	
Number of patients	22
Median (range)	0.3 (0.0 - 0.9)
Any post-transplant maintenance	
No	31 (15)
Yes	182 (85)
Maintenance therapy, n (%)	
Len +/- Dex	105 (49)
Len + PI +/- Dex	29 (14)
Len/Elotuzumab	21 (10)
Single agent PI	23 (11)
Other/unknown	35 (16)

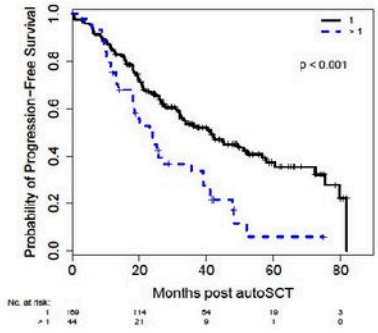

Figure 1. Progression-free survival in patients with (1) or (>1) additional copies of 1q

Abbreviations: n = number; autoSCT = autologous hematopoietic stem cell transplant; NA = not available; R-ISS = Revised International Staging System; ISS = International Staging System; KRD = carfilzomib, lenalidomide, dexamethasone; VCD = bortezomib, cyclophosphamide, dexamethasone; VD = bortezomib, dexamethasone; VRD = bortezomib, lenalidomide, dexamethasone; Bu/Mel = busulfan, melphalan; Mel = melphalan; CR = complete response; sCR = stringent complete response; nCR = near complete response; VGPR = very good partial response; PR = partial response; SD = stable disease; PD = progressive disease; MRD = minimal residual disease; Len = lenalidomide; Dex = dexamethasone; PI = proteasome inhibitor.

Figure 1

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