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POSTER ABSTRACTS

731.AUTOLOGOUS TRANSPLANTATION: CLINICAL AND EPIDEMIOLOGICAL

Trends in Outcomes over Three Decades after Upfront Autologous Stem Cell Transplant for Multiple Myeloma at MD Anderson Cancer Center

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Introduction

Remarkable advances have been made in the treatment of multiple myeloma (MM) with the advent of novel therapies and the use of post-transplant maintenance. We report trends in outcomes of MM patients who received upfront autologous hematopoietic stem cell transplantation (autoHCT) at our institution over more than three decades.

Methods

We conducted a single-center retrospective study of patients with newly diagnosed MM undergoing upfront autoHCT between 1988 to 2021. Patients were grouped by the year of autoHCT: 1988-2000 (n=249), 2001-2005 (n=373), 2006-2010 (n=568), 2011-2015 (n=815) and 2016-2021 (n=1036). High-risk cytogenetic abnormalities were defined as del17p, t(4;14), t(14;16), 1q21 gain or amplification by fluorescence in situ hybridization. Progression free survival (PFS) and overall survival (OS) were estimated using the Kaplan-Meier method, and group differences were assessed using the log-rank test. Associations between demographic and clinical factors and survival outcomes were evaluated using Cox proportional hazards regression analysis.

Results

A total of 3041 patients were included in our analysis. Median age at autoHCT increased from 52 years (1988-2000) to 62 years (2016-2021), with only 1% of transplanted patients being ≥ 65 years of age in 1988-2000, compared to 38% in 2016-2021 (p<0.001). The proportion of African-American patients increased from 9% in 1988-2000 to 19% in 2016-2021 (p=0.004). The incidence of high-risk cytogenetics increased from 15% in 1988-2000 to 40% in 2016-2021 (p<0.001). The comorbidity burden, as measured by the hematopoietic cell transplantation-specific comorbidity index (HCT-CI), increased over time, with 17% of patients having HCT-CI>3 in 1988-2000 compared to 28% in 2016-2021 (p<0.001). Induction regimens evolved over time from predominately conventional chemotherapy (39%) in 1988-2000 to immunomodulatory drug (IMiD) and proteasome inhibitor (PI)-based regimens, with 74% receiving an IMiD-PI containing triplet [39% bortezomib, lenalidomide and dexamethasone (VRD) and 35% carfilzomib, lenalidomide and dexamethasone (KRD)] between 2016-2021 (p<0.001). Maintenance therapy was used in >80% from 2011 onwards (Table 1).

Response rates prior to autoHCT steadily improved with 4% and 10% patients achieving ≥CR and ≥VGPR between 1988-2000, compared to 19% and 65% between 2016-2021, respectively. At day 100 post-transplant, 24% and 49% patients achieved ≥CR and ≥VGPR between 1988-2000 compared to 41% and 81% between 2016-2021, respectively. At best post-transplant response, 33% and 53% patients achieved ≥CR and ≥VGPR between 1988-2000 compared to 63% and 91% between 2016-2021, respectively.

The median PFS in the entire study population was 38.3 months (95% CI 36.4-40.3), improving from 22.3 months between 1988-2000 to 58.6 months between 2016-2021 (hazard ratio [95% CI]: 0.42 [0.36-0.50], p<0.001; Figure 1A). Notably, patients

with high-risk cytogenetics also had an improvement in PFS in recent years, with a median PFS of 28.0 months (0.38 [0.26-0.55], p<0.001) and 36.8 months (0.32 [0.22-0.46], p<0.001) in 2011-2015 and 2016-2021, respectively, compared to only 13.7 months in 2001-2005. Patients aged ≥65 years also had an improvement in median PFS from 33.6 months (95% CI 23.1-44.2) between 2001-2005 to 52.8 months (95% CI 40.0-68.5, p<0.001) between 2016-2021.

Median OS was 99.4 months (95% CI 94.2-104.0) in the entire study population, steadily improving from 55.1 months to not reached (0.41 [0.33-0.52], p<0.001) in 1988-2000 and 2016-2021, respectively (Figure 1B). Similarly, in those with high-risk cytogenetics, OS improved with a median OS of 32.9 months in 2001-2005 compared to 66.5 months (0.39 [0.26-0.61], p<0.001) in 2016-2021. Between 1988-2000, day 100 non-relapse mortality (NRM) was 6%, whereas from 2001 onwards NRM remained ≤ 1% (p<0.001).

Conclusions

This single-center analysis of over 3,000 newly diagnosed MM patients undergoing upfront autoHCT demonstrates significant improvements in the depth of response and survival outcomes over the past three decades, even in patients with high-risk disease. NRM remained <1% despite increasing age and comorbidity burden.

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Table 1. Patient characteristics

Variable	Time Period					p-value
	1988-2000 (N=249)	2001-2005 (N=373)	2006-2010 (N=568)	2011-2015 (N=815)	2016-2021 (N=1,036)	
Gender, n (%)						
Male	166 (67)	224 (60)	333 (59)	468 (57)	622 (60)	0.13
Female	83 (33)	149 (40)	235 (41)	347 (43)	414 (40)	
Age at autoHCT (years)						
Median (range)	51.7 (22.7, 70.9)	55.8 (29.4, 77.4)	59.6 (31.0, 80.6)	61.6 (25.4, 80.3)	62.3 (29.0, 83.0)	<0.001
Age, n (%)						
<65 years	247 (99)	327 (88)	413 (73)	526 (65)	638 (62)	<0.001
≥65 years	2 (1)	46 (12)	155 (27)	289 (35)	398 (38)	
Race, n (%)						
Black	22 (9)	63 (17)	95 (17)	141 (18)	198 (19)	0.004
non-black	224 (91)	307 (83)	463 (83)	655 (82)	822 (81)	
Light chain type, n (%)						
Kappa	142 (65)	228 (62)	371 (66)	532 (66)	682 (66)	0.11
Lambda	73 (33)	137 (37)	191 (34)	272 (34)	346 (34)	
Biclonal	4 (2)	3 (1)	3 (1)	7 (1)	1 (<1)	
Cytogenetic risk, n (%)						
Standard	47 (85)	254 (87)	474 (93)	605 (78)	582 (60)	<0.001
High	8 (15)	38 (13)	37 (7)	168 (22)	389 (40)	
Unknown	194	81	57	42	65	
R-ISS, n (%)						
I	8 (21)	32 (34)	88 (35)	203 (37)	268 (34)	0.54
II	26 (68)	55 (59)	142 (57)	299 (55)	443 (56)	
III	4 (11)	7 (7)	21 (8)	45 (8)	83 (10)	
Unknown	211	279	317	268	242	
HCTCI, n (%)						
≤3	53 (83)	304 (82)	444 (78)	637 (78)	742 (72)	<0.001
>3	11 (17)	69 (19)	123 (22)	177 (22)	293 (28)	
Induction regimen, n (%)						
Chemotherapy	98 (40)	81 (22)	20 (4)	32 (4)	7 (1)	<0.001
Imid-based Doublets	4 (2)	198 (53)	216 (38)	64 (8)	19 (2)	
KRD	0	0	0	2 (<1)	362 (35)	
VCD	0	0	45 (8)	155 (19)	101 (10)	
VD	0	2 (1)	107 (19)	167 (20)	64 (6)	
VRD	0	0	60 (11)	298 (37)	407 (39)	
Other	146 (59)	91 (24)	120 (21)	97 (12)	75 (7)	
Unknown	1	1	0	0	1	
Response before autoHCT, n (%)						
sCR/CR	9 (4)	29 (8)	39 (7)	89 (11)	197 (19)	<0.001
nCR/VGPR	16 (6)	62 (17)	237 (42)	333 (41)	479 (46)	
PR	134 (54)	235 (63)	277 (49)	375 (46)	339 (33)	
SD	87 (35)	44 (12)	15 (3)	18 (2)	21 (2)	
PD	1 (<1)	3 (1)	0	0	0	
Conditioning regimen, n (%)						
Mel	55 (22)	297 (80)	495 (87)	708 (87)	780 (75)	<0.001
Mel-based other	70 (28)	70 (19)	44 (8)	13 (2)	44 (4)	
BuMel based	0	6 (2)	29 (5)	94 (12)	182 (18)	
Thiotepa/Bu/Cy	118 (47)	0	0	0	0	
Other	6 (2)	0	0	0	30 (3)	
Any maintenance, n (%)						
Yes	181 (73)	112 (30)	231 (41)	673 (83)	848 (82)	<0.001
No	68 (27)	261 (70)	337 (59)	142 (17)	188 (18)	
Maintenance, n (%)						
Len +/-Dexa	0	6 (6)	173 (77)	515 (77)	664 (79)	<0.001
Imid +/-Dexa	40 (25)	66 (69)	43 (19)	3 (<1)	6 (1)	
PI +/-Dexa	0	3 (3)	9 (4)	63 (9)	69 (8)	
Other	118 (75)	21 (22)	0	88 (13)	106 (13)	

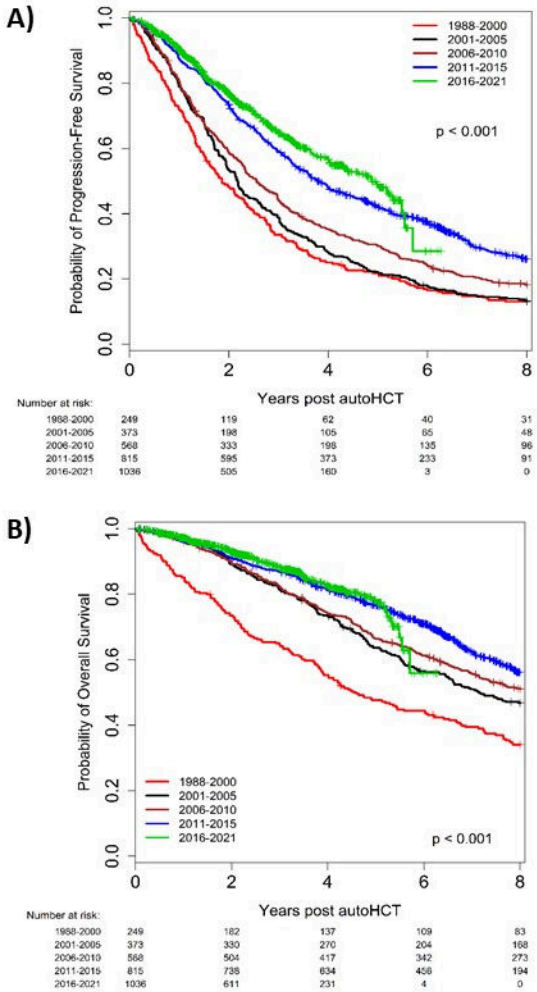

Figure 1. Progression-free survival (A) and overall survival (B) according to year of autoHCT

Abbreviations: AutoHCT=autologous hematopoietic stem cell transplantation; Bu/Cy=busulfan/cyclophosphamide; BuMel=busulfan+melphalan; CR=complete response; Dexa=dexamethasone; HCT-CI=hematopoietic cell transplantation-specific comorbidity Index; Imid=immunomodulatory drug; KRD=carfilzomib+lenalidomide+dexamethasone; Len=lenalidomide; Mel=melphalan; nCR=near complete response; PD=progressive disease; PI=proteasome inhibitor; PR=partial response; R-ISS=revised international Staging System; sCR=stringent complete response; SD=stable disease; VCD=bortezomib+cyclophosphamide+dexamethasone; VD= bortezomib+dexamethasone; VGPR=very good partial response; VRD=bortezomib+lenalidomide+dexamethasone.

Figure 1