Original Article

Hispanics Have the Lowest Stem Cell Transplant Utilization Rate for Autologous Hematopoietic Cell Transplantation for Multiple Myeloma in the United States: A CIBMTR Report

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BACKGROUND: Race/ethnicity remains an important barrier in clinical care. The authors investigated differences in the receipt of autologous hematopoietic cell transplantation (AHCT) among patients with multiple myeloma (MM) and outcomes based on race/ethnicity in the United States. **METHODS:** The Center for International Blood and Marrow Transplant Research database was used to identify 28,450 patients who underwent AHCT for MM from 2008 through 2014. By using data from the National Cancer Institute's Surveillance, Epidemiology, and End Results 18 registries, the incidence of MM was calculated, and a stem cell transplantation utilization rate (STUR) was derived. Post-AHCT outcomes were analyzed among patients ages 18 to 75 years who underwent melphalan-conditioned peripheral cell grafts (N = 24,102). **RESULTS:** The STUR increased across all groups from 2008 to 2014. The increase was substantially lower among Hispanics (range, 8.6%-16.9%) and non-Hispanic blacks (range, 12.2%-20.5%) compared with non-Hispanic whites (range, 22.6%-37.8%). There were 18,046 non-Hispanic whites, 4123 non-Hispanic blacks, and 1933 Hispanic patients. The Hispanic group was younger ($P < .001$). Fewer patients older than 60 years underwent transplantation among Hispanics (39%) and non-Hispanic blacks (42%) compared with non-Hispanic whites (56%). A Karnofsky score <90% and a hematopoietic cell transplantation comorbidity index score >3 were more common in non-Hispanic blacks compared with Hispanic and non-Hispanic whites ($P < .001$). More Hispanics (57%) versus non-Hispanic blacks (54%) and non-Hispanic whites (52%; $P < .001$) had stage III disease. More Hispanics (48%) versus non-Hispanic blacks (45%) and non-Hispanic whites (44%) had a very good partial response or better before transplantation ($P = .005$). Race/ethnicity did not impact post-AHCT outcomes. **CONCLUSIONS:** Although the STUR increased, it remained low and was significantly lower among Hispanics followed by non-Hispanic blacks compared with non-Hispanic whites. Race/ethnicity did not impact transplantation outcomes. Efforts to increase the rates of transplantation for eligible patients who have MM, with an emphasis on groups that underuse transplantation, are warranted. ***Cancer* 2017;123:3141-9**. © *2017 American Cancer Society.*

KEYWORDS: blacks, Hispanic, myeloma, transplantation utilization.

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INTRODUCTION

Recent studies have confirmed the role of upfront autologous hematopoietic cell transplantation (AHCT) in patients with newly diagnosed multiple myeloma (MM), even in the age of novel induction therapies.[1-4] Despite these data and continued recommendations from the National Comprehensive Cancer Center (NCCN) that transplantation should be considered in patients who have symptomatic disease,[5] studies from the United States suggest that only approximately 30% of patients with MM undergo transplantation.[6-8] Understanding barriers is critical to developing strategies to increase the use of AHCT as a therapeutic option.

The role of race in the receipt and efficacy of AHCT among patients with MM has been previously studied.[8-10] Despite a significantly higher incidence of MM among blacks compared with whites, these studies have demonstrated lower utilization rates in blacks. It is noteworthy that studies have also demonstrated no differences in outcomes, such as treatment-related mortality and survival after AHCT for MM, based on race.[9,10]

Data are sparse on the use and efficacy of AHCT in other ethnic groups, especially among patients who self-identify as Hispanic, which is the fastest growing segment of the population in the United States. We used the Center for International Blood and Marrow Transplant Research (CIBMTR) and Surveillance, Epidemiology and End Results (SEER) databases to identify differences in transplantation receipt and outcomes in self-identified racial and ethnic groups among patients with MM who underwent AHCT in the United States.

MATERIALS AND METHODS

Data Source

The CIBMTR registry is a prospectively maintained transplantation database that collects transplantation data from over 450 centers worldwide. Data are submitted to the Statistical Center at the Medical College of Wisconsin in Milwaukee, where computerized checks for discrepancies, physicians' review of submitted data, and on-site audits of participating centers ensure data quality. Collected data include disease type, age, sex, self-identified race/ethnicity, date of diagnosis, graft type, conditioning regimen, post-transplantation disease progression, survival, and cause of death and along with all transplantations reported to the CIBMTR. Data are collected before transplantation, 100 days and 6 months after transplantation, and annually thereafter until death or last follow-up. Between 2008 and 2014, the CIBMTR captured from 75% to 80% of all autologous transplantations performed in the United States. For the purposes of this study, it was assumed that there was no systematic age, sex, or race/ethnicity biases in reporting AHCT to the CIBMTR.

Patients

All US patients registered with the CIBMTR for a first AHCT for MM during the period from 2008 to 2014 were collected (N = 28,450) and used to determine the stem cell transplantation utilization rate (STUR). Only first transplantations were counted. Among these, patients ages 18 to 75 years who underwent peripheral hematopoietic cells with melphalan conditioning, provided informed consent, and had a 100-day follow-up form reported were included in the descriptive and multivariate analyses (N = 24,102).

The incidence of MM was obtained from the National Cancer Institute's SEER Program. SEER data are derived from registries covering approximately 27.8% of the US population; we used the SEER 18 database, which contains patients diagnosed from 2002 through 2013. By using publicly available software, which also provides US population estimates (SEER*Stat[11]), we calculated incidence rates per 100,000 persons for the years 2008 through 2013. SEER provides information according to race and ethnicity, yielding the categorization of individuals as Hispanics (irrespective of race), non-Hispanic blacks, and non-Hispanic whites. For patients with MM, SEER provides information on age at diagnosis, sex, and prior and subsequent malignancies, but not on staging, biologic characteristics (including chromosome abnormalities), or the receipt of systemic therapy, including hematopoietic cell transplantation (HCT). We combined MM incidence derived from the SEER program with transplantation activity reported to the CIBMTR for the period from 2008 to 2013 to assess the impact of disparities in AHCT.

Statistical Analysis

An estimate of the transplantation rate was calculated. This STUR was defined as the number of new AHCTs in a given year divided by the number of patients with newly diagnosed MM for that year. The number of new AHCTs each year was calculated as the number of AHCTs reported to the CIBMTR divided by the CIBMTR capture rate. Because the estimated CIBMTR capture rate during this time ranged from 75% to 80%, a sensitivity analysis was performed to provide a range to the rate of ±5% for the CIBMTR AHCT transplantation capture rate in each year.

TABLE 1. Stem Cell Transplantation Utilization Rates in Patients With Multiple Myeloma

	Hispanic		Non-Hispanic Black		Non-Hispanic White		
Year	Incidence (95% CI)	STUR Estimate (95% CI), %	Incidence (95% CI)	STUR Estimate (95% CI), %	Incidence (95% CI)	STUR Estimate (95% CI), %	Overall STUR Estimate (95% CI), %
2008	5.8 (5.3-6.3)	8.6 (7.9-9.4)	12.6 (11.7-13.4)	12.2 (11.4-13)	5.7 (5.5-5.9)	22.6 (21.8-23.9)	19.1 (18.5-19.6)
2009	5.9 (5.4-6.4)	9.8 (9.0-10.7)	12.9 (12.1-13.8)	13.2 (12.4-14)	5.7 (5.5-5.9)	26.6 (25.7-27.5)	21.9 (21.3-22.5)
2010	6.0 (5.5-6.5)	11.9 (10.9-13)	12.9 (12.2-13.8)	15.7 (14.8-16.8)	6.0 (5.8-6.2)	29.4 (28.4-30.4)	24.7 (24.1-25.4)
2011	6.3 (5.9-6.9)	11.4 (10.6-12.4)	13.3 (12.5-14.1)	18.2 (17.1-19.3)	5.9 (5.7-6.1)	34 (32.9-35.1)	27.8 (27.1-28.6)
2012	6.2 (5.7-6.7)	14.2 (13.1-15.4)	13.7 (12.9-14.5)	19 (18-20.2)	6.0 (5.8-6.2)	35.4 (34.3-36.6)	29.5 (28.8-30.3)
2013	5.6 (5.2-6.1)	16.9 (15.6-18.3)	13.3 (12.5-14.1)	20.5 (19.4-21.8)	5.8 (5.6-6.0)	37.8 (35.5-38)	30.8 (30-31.6)

Abbreviations: CI, confidence interval STUR, stem cell transplantation utilization rate.
[a] The incidence rate is age-adjusted and shown per 100,000 population, and the STUR is expressed as a percentage; both rates include 95% CIs in parentheses.

Patient-related, disease-related, and treatment-related factors were compared using the chi-square test for categorical variables and the Kruskal-Wallis test for continuous variables. The outcomes analyzed included transplantation-related mortality, relapse/progression, progression-free survival, and overall survival (OS). Estimates of outcomes were reported as probabilities with 95% confidence intervals (CIs). The probability of OS was calculated using the Kaplan-Meier estimator, and variance was estimated with the Greenwood formula. Survival curves were compared using the log-rank test. Multivariate analysis on OS was performed using a Cox proportional-hazards model with race/ethnicity as the main effect. We explored interactions between the main effect and the variables in the final model. The assumption of proportional hazards was tested for each variable, and factors that violated the proportionality assumption were adjusted by stratification. Potential interactions between the main effect and all other significant risk factors were tested. All P values are 2-sided; and, given the large sample size, P values $< .01$ were considered significant, a priori.

RESULTS

Table 1 shows the incidence rate of MM calculated using the SEER database for the years 2008-2013. Next, the STUR was calculated (Supporting Table 1; see online supporting information). The incidence of MM in the Hispanic and non-Hispanic white groups remained stable during this period at an incidence rate of 5.6 to 6.3 per 100,000 for Hispanics and 5.7 to 6.0 per 100,000 for non-Hispanic whites. In the non-Hispanic black group, the incidence of MM was nearly double at 12.7 to 13.7 per 100,000 during this period. The overall STUR estimate was 19.1% (95% CI, 18.5%-19.6%) in 2008 and increased to 30.8% (95% CI, 30%-31.6%) in 2013. When parsed between the 3 racial/ethnic groups, the STUR estimate increased across all 3 groups from 8.6% (95% CI, 7.9%-9.4%) in 2008 to 16.9% (95% CI, 15.6%-18.3%) in 2013 for Hispanics, from 12.2% (95% CI, 11.4%-13%) in 2008 to 20.5% (95% CI, 19.4%-21.8%) in 2013 for non-Hispanic blacks, and from 22.6% (95% CI, 21.8%-23.9%) in 2008 to 37.8% (95% CI, 35.5%-38%) in 2013 for non-Hispanic whites.

Table 2 lists the characteristics of 24,102 patients ages 18 to 75 years who underwent a first AHCT for MM that was reported to the CIBMTR between 2008 and 2014, received melphalan conditioning and underwent a peripheral HCT, and had at least 100 days of follow-up using CIBMTR registration-level data, which captured from 75% to 80% of MM AHCT activity in the United States during the period. In this cohort, we identified 18,046 non-Hispanic whites, 1933 Hispanics, and 4123 non-Hispanic blacks who underwent transplantation.

There were significant differences in pretransplantation characteristics between groups. The Hispanic group was younger, with a median age of 57 years (range, 19-75 years) versus non-Hispanic blacks (median age, 58 years; range, 20-75 years) and non-Hispanic whites (median age, 61 years; range, 19-75 years; $P < .001$). Fewer patients aged >60 years underwent transplantation in the Hispanic (39%) and non-Hispanic black (42%) groups versus the non-Hispanic white group (56%; $P < .001$). More women than men underwent transplantation in the non-Hispanic black (50%) and Hispanic (43%) groups versus the non-Hispanic white group (41%; $P < .001$). A greater proportion of non-Hispanic blacks (44%) had lower Karnofsky scores (<90%) compared with Hispanics and non-Hispanic whites (39% each; $P < .001$). Similarly, a higher proportion of non-Hispanic blacks (38%)

TABLE 2. Patient Characteristics (N = 24,102)

Variable	No. of Patients (%)			*P*
	Hispanic	Non-Hispanic Black	Non-Hispanic White	
No. of enrolled patients	1933	4123	18046	
No. of centers	111	126	135	
Patient-related variables				
Age at transplantation: Median [range], y	57 [19-75]	58 [20-75]	61 [19-75]	< .001
<45	213 (11)	395 (10)	838 (5)	
45-60	972 (50)	2003 (49)	7164 (40)	
61-75	748 (39)	1725 (42)	10044 (56)	
Sex, men	1097 (57)	2062 (50)	10693 (59)	< .001
Karnofsky score <90%	750 (39)	1807 (44)	7116 (39)	< .001
HCT-CI index				< .001
No comorbidity	618 (32)	920 (22)	5043 (28)	
1-2	639 (33)	1241 (30)	5353 (30)	
≥3	465 (24)	1587 (38)	6209 (34)	
Missing	211 (11)	375 (9)	1441 (8)	
Disease-related variables				
Immunochemical subtype				< .001
IgG	1055 (55)	2652 (64)	10154 (56)	
IgA	410 (21)	662 (16)	3899 (22)	
Light chain	399 (21)	725 (18)	3469 (19)	
Nonsecretory	41 (2)	61 (1)	302 (2)	
Others	28 (1)	22 (<1)	221 (1)	
Missing	0	1 (<1)	1 (<1)	
Advanced stage at diagnosis: ISS/DSS III	1100 (57)	2216 (54)	9379 (52)	< .001
Time from diagnosis to transplantation, mo				< .001
<6	436 (23)	860 (21)	5454 (30)	
6-12	860 (44)	1839 (45)	7864 (44)	
>12	634 (33)	1420 (34)	4699 (26)	
Missing	3 (<1)	4 (<1)	29 (<1)	
Transplantation-related variables				
Melphalan dose 200 mg/m^2	1636 (85)	3488 (85)	15469 (86)	.29
Disease status before transplantation				.005
sCR/CR	315 (16)	571 (14)	2551 (14)	
VGPR	611 (32)	1260 (31)	5388 (30)	
PR	787 (41)	1809 (44)	8079 (45)	
SD/relapse/progression	212 (11)	476 (12)	1953 (11)	
Missing	8 (<1)	7 (<1)	75 (<1)	
Planned post-transplantation therapy				< .001
No	1571 (81)	3205 (78)	13426 (74)	
Yes	360 (19)	914 (22)	4585 (25)	
Missing	2 (<1)	4 (<1)	35 (<1)	
Follow-up of survivors: Median [range], mo	36 (1-99)	37 (1-97)	38 (1-98)	

Abbreviations: CR, complete response; DSS, Durie-Salmon staging; HCT-CI, hematopoietic cell transplantation-comorbidity index; IgA, immunoglobulin A; IgG, immunoglobulin G; ISS, International Staging System; PR, partial response; SD, stable disease; sCR, stringent complete response; VGPR, very good partial response.

and non-Hispanic whites (34%) had higher HCT-comorbidity index (HCT-CI) scores ≥3 compared with Hispanics (24%; $P < .001$). Advanced disease stage (Durie-Salmon or International Staging System stage III) was more common among the Hispanic (57%) and non-Hispanic black (54%) groups versus the non-Hispanic white group (52%; $P < .001$). A greater proportion of non-Hispanic whites proceeded to transplantation <6 months after diagnosis (30%) compared with Hispanics (23%) and non-Hispanic blacks (21%; $P < .001$). More Hispanics (48%) patients were in a very good partial response (VGPR) or better disease status at the time of AHCT compared with non-Hispanic black patients (45%) and non-Hispanic white patients (44%; $P < .005$).

Next, we characterized further details of the 1933 Hispanic patients who proceeded to transplantation (Table 3). The majority (N = 1590) identified as Hispanic white, 64 identified as Hispanic black, and 279 as identified as Hispanic other. There were no differences between these groups noted for age, sex, Karnofsky score, HCT-CI score, time to transplantation, or pretransplantation staging. There were more patients with stage III disease in the Hispanic white group (59%) compared with the Hispanic black (55%) and Hispanic other groups (47%; $P = .008$).

TABLE 3. Characteristics of Hispanic patients (N = 1933)

Variable	No. of Patients (%)			P
	Hispanic White	Hispanic Black	Hispanic Others	
No. of enrolled patients	1590	64	279	
No. of centers	102	32	54	
Patient-related variables				
Age at transplantation: Median [range], y	57 [19-75]	57 [40-74]	57 [28-74]	.46
<45	184 (12)	4 (6)	25 (9)	
45-60	793 (50)	32 (50)	147 (53)	
61-75	613 (39)	28 (44)	107 (38)	
Sex, men	907 (57)	30 (47)	160 (57)	.27
Karnofsky score <90%	621 (39)	28 (44)	101 (36)	.72
HCT-CI index				.09
No comorbidity	502 (32)	19 (30)	97 (35)	
1-2	524 (33)	15 (23)	100 (36)	
≥3	381 (24)	23 (36)	61 (22)	
Missing	183 (12)	7 (11)	21 (8)	
Clinical trial enrollment	51 (3)	1 (2)	13 (5)	.33
Disease-related variables				
Immunochemical subtype				.67
IgG	862 (54)	36 (56)	157 (56)	
IgA	340 (21)	11 (17)	59 (21)	
Light chain	332 (21)	15 (23)	52 (19)	
Nonsecretory	35 (2)	2 (3)	4 (1)	
Others	21 (1)	0	7 (3)	
ISS/DSS III	934 (59)	35 (55)	131 (47)	.008
Time from diagnosis to transplantation, mo				.52
<6	369 (23)	12 (19)	55 (20)	
6-12	711 (45)	26 (41)	123 (44)	
>12	508 (32)	26 (41)	100 (36)	
Missing	2	0	1	
Transplantation-related variables				
Melphalan dose 200 mg/m^2	1336 (84)	51 (80)	249 (89)	.04
Disease status before transplantation				.98
sCR/CR	259 (16)	10 (16)	46 (16)	
VGPR	499 (31)	18 (28)	94 (34)	
PR	653 (41)	27 (42)	107 (38)	
SD/relapse/progression	172 (11)	9 (14)	31 (11)	
Missing	7 (<1)	0	1 (<1)	
Planned post-transplantation therapy				.03
No	1294 (81)	60 (94)	217 (78)	
Yes	295 (19)	4 (6)	61 (22)	
Missing	1 (<1)	0	1 (<1)	
Follow-up of survivors: Median [range], mo	37 [1-99]	37 [4-74]	25 [1-82]	

Abbreviations: CR, complete response; DSS, Durie-Salmon staging; HCT-CI, hematopoietic cell transplantation-comorbidity index; IgA, immunoglobulin A; IgG, immunoglobulin G; ISS, International Staging System; PR, partial response; SD, stable disease; sCR, stringent complete response; VGPR, very good partial response.

Post-transplantation outcomes are detailed in Table 4. No difference was observed between the different racial and ethnic groups for transplantation-related mortality, progression-free survival, or OS (Fig. 1). On multivariate analysis (Table 5), race and ethnicity had no influence on survival (Table 5); however older age (range, 61-75 years), male sex, a Karnofsky score <90%, an HCT-CI score ≥3, a longer interval from diagnosis to transplantation (>12 months), a lower melphalan dose for conditioning (140 mg/m^2), and adverse disease status (complete response or worse) before transplantation adversely affected survival.

DISCUSSION

MM is 1 of the model cancers in which survival for patients has increased considerably during the first decade of the 21st century. However, this improvement has not increased across all racial/ethnic strata in the United States. Multiple studies have demonstrated disparities in outcomes among patients with MM using SEER data. Pulte et al reported an improvement in age-adjusted, 5-year relative survival for patients with MM, with an increase from 35.6% during 1998 through 2001 to 44% during 2006 through 2009.[12] However, this increase was greatest for non-Hispanic whites, and excess mortality

TABLE 4. Univariate Outcomes of Patients Characterized by Race and Ethnicity (N = 24,102)

	Hispanic, N = 1933		Non-Hispanic Black, N = 4123		Non-Hispanic White, N = 18,046		
Outcome	No. of Patients	Prob (95% CI), %	No. of Patients	Prob (95% CI), %	No. of Patients	Prob (95% CI), %	*P*
NRM	1926		4104		18,006		.36[a]
100-Day		0.6 (0.3-1)		0.6 (0.4-0.9)		0.9 (0.7-1)	.15
1-Year		2 (2-3)		3 (2-3)		3 (2-3)	.70
PFS	1926		4104		18,006		1.0[a]
1-Year		82 (80-84)		82 (81-83)		83 (82-83)	.30
2-Year		66 (64-68)		66 (64-67)		66 (65-67)	.93
3-Year		54 (51-56)		54 (52-55)		53 (52-54)	.84
OS	1932		4120		18,030		.13[a]
1-Year		94 (93-95)		94 (94-95)		94 (93-94)	.26
2-Year		86 (85-88)		86 (85-87)		86 (85-86)	.72
3-Year		80 (77-82)		79 (77-80)		77 (77-78)	.05

Abbreviations: CI, confidence interval; NRM, nonrelapse mortality; OS, overall survival; PFS, progression-free survival; Prob, probability.
[a] log rank *p*-value.

TABLE 5. Multivariate Analysis of Overall Survival

Effect	HR (95% CI)	*P*
Main effect		.08
Hispanic	1.00	
Non-Hispanic black	0.99 (0.89-1.11)	.2
Non-Hispanic white	1.07 (0.97-1.18)	.9
Age, y		< .0001
<45	1.00	
45-60	1.15 (1.02-1.30)	.02
61-75	1.33(1.18-1.50)	< .0001
Sex		< .0001
Men	1.00	
Women	0.87 (0.823-0.92)	
Karnofsky score		< .0001
≥90%	1.00	
<90%	1.23 (1.19-1.32)	
Missing	1.14 (1.01-1.29)	
HCT-CI		<.0001
No comorbidity	1.00	
1-2	1.04 (0.97-1.11)	.26
≥3	1.21 (1.13-1.29)	< .0001
Missing	0.87 (0.79-0.96)	.006
Stage at diagnosis		< .0001
<III	1.00	
III	1.46 (1.39-1.54)	< .0001
Missing	1.17 (1.02-1.34)	.02
Time from diagnosis to transplantation, mo		< .0001
<6	1.00	
6-12	1.08 (1.01-1.15)	.03
>12	1.44 (1.34-1.54)	< .0001
Missing	2.13 (1.28-3.55)	.004
Melphalan dose, mg/m^2		< .0001
140	1.00	
200	0.85 (0.80-0.91)	< .0001
Missing	0.41 (0.06-2.93)	.4
Disease status at transplantation		< .0001
sCR/CR	1.00	
VGPR	1.22 (1.11-1.33)	< .0001
PR	1.32 (1.22-1.44)	< .0001
SD/relapse/progression	2.04 (1.84-2.25)	< .0001
Missing	1.39 (0.85-2.28)	.2

Abbreviations: CI, confidence interval; CR, complete response; HCT-CI, hematopoietic cell transplantation-comorbidity index; HR, hazard ratio; PR, partial response; SD, stable disease; sCR, stringent complete response; VGPR, very good partial response.

hazard ratios were observed among non-Hispanic blacks and Hispanics compared with non-Hispanic whites,[12] suggesting that ethnic minorities may have not benefited from the advances in MM therapies to a similar extent as non-Hispanic whites. Ailawadhi et al also reported similar findings using SEER 17 registry data.[13]

Although AHCT is not a new therapy in MM, despite the availability of several novel therapies, it remains an important treatment option, especially in the upfront setting, based on numerous recent studies.[1-3,14] We conducted the current research to better understand disparities in transplantation use in the United States. In this large database study, which captures the majority of MM AHCT activity in the United States, we make the following observations: 1) The STUR in MM has improved significantly from 2008 to 2013; 2) however, despite the increase, the overall STUR was only 30.8% in 2013 and was lowest among Hispanics followed by non-Hispanic blacks and was highest among non-Hispanic whites; 3) Hispanic patients who undergo AHCT for MM tend to be younger, fitter, and have more advanced disease; and 4) race/ethnicity did not impact post-AHCT MM outcomes.

Despite compelling evidence and NCCN recommendations[5] that patients with MM should be evaluated at a stem cell transplantation center, the rate of transplantation use remained low, at approximately 30.8% in 2013. Despite an almost doubling of the STUR from 8.6% to 16.9% among Hispanics and a 70% increase in the STUR among blacks from 12.2% to 20.5%, the rate remained substantially lower than that among non-Hispanic whites, for whom it rose from 22.6% to 37.8% in the same time frame. In addition, the increased rate of patients who underwent transplantation from 2008 to

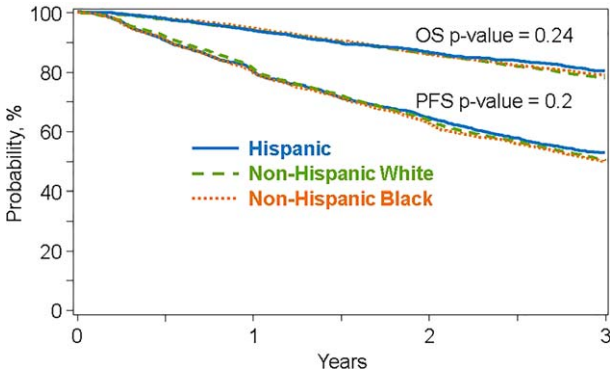

Figure 1. Progression-free survival (PFS) and overall survival (OS) are illustrated by race/ethnicity.

2013 was far greater in non-Hispanic whites (15.2%), versus non-Hispanic blacks (8.3%) and Hispanics (8.3%). This means that Hispanic patients undergo transplantation at less than one-half the rate of non-Hispanic white patients (45%), and non-Hispanic black patients undergo transplantation at a just over one-half the rate (54%) of non-Hispanic white patients. Others have also reported that non-Hispanic black and Hispanic patients with MM have a lower rate of AHCT.[6,8] Al-Hamadani et al demonstrated that older age, lower levels of education and household income, nonmanaged health care, residence in a metropolitan area, treatment at a community center, a treatment facility outside the Midwest and Western regions, as well as racial and ethnic minorities are all less likely to predict receipt of AHCT for patients with MM.[6] Joshua et al previously demonstrated that transplantation, both autologous and allogeneic, is more frequently received by white patients than by black patients for the treatment of treat leukemia, lymphoma and MM.[10]

Our data also indicate that there are differences according to race/ethnicity in the profiles of patients who receive AHCT for MM. Hispanic and non-Hispanic black patients tend to be younger, and few patients aged >60 years undergo transplantation in these groups compared with the non-Hispanic white group. This is particularly poignant in patients with MM, because the median age at diagnosis of MM is 69 years.[15] This finding may also account in part for some differences in the STUR across race/ethnicities. Hispanic and non-Hispanic black patients were also more likely to have advanced-stage disease at diagnosis and to undergo transplantation later from diagnosis than non-Hispanic white patients. This confirms the results of a small, single-center study from Baltimore indicating that, among patients with MM who were referred for AHCT, black patients were younger and often had delayed referrals for AHCT compared with white patients.[16] We now extend this finding to Hispanic patients as well.

A significantly higher percentage of Hispanic patients had lower comorbidity scores and were more likely to have a better disease status (VGPR or better) before transplantation compared with non-Hispanic black and non-Hispanic white patients. This suggests that Hispanic patients who undergo transplantation tend to be younger, fitter, have more advanced but responsive disease, and undergo transplantation later in their disease course than non-Hispanic white patients. Non-Hispanic black recipients of AHCT also have a similar profile; they too are younger, have more advanced disease, and undergo transplantation later than non-Hispanic white patients. In addition, they are more likely to have higher comorbidities than non-Hispanic white and Hispanic patients. Fiala et al demonstrated that the racial disparities between black and white patients with MM who undergo AHCT are not fully accounted for by age, sex, socioeconomic status, insurance, and comorbidities.[17] The Institute of Medicine has also reported that racial and ethnic disparities in health care are not entirely explained by differences in access to care, clinical appropriateness, or patient preferences.[18] Studies have also documented differential receipt of technical aspects of care, such as tests, therapies, and procedures, among racial/ethnic minorities compared with whites, even after controlling for insurance status and access to medical care.[19] These data point toward an interplay of many other complex factors, such as physician bias, referral bias, cultural beliefs, language barriers, and access to a transplantation center, which may affect the receipt of AHCT among different race/ethnic groups. One single-center study demonstrated that, once patients attend a transplantation center, transplantation rates are similar among different ethnic groups.[20] In another setting, namely, the treatment of patients with MM in clinical trials in the United States, a similar difference has been reported.[21]

Previous literature, including reports from the CIBMTR, has indicated that post-transplantation outcomes are identical regardless of race.[9,16,22] Our current results extend that literature among ethnic subgroups with identical results. With this in mind, and recognizing the differences in the STUR, we believe it is time for a concerted effort to improve the STUR among all groups, with special emphasis on the low-performing ethnicities. NCCN and other national guidelines could address the finding that outcomes for similarly treated patients are

comparable across racial and ethnic groups, but the STUR varies.

Our data have some limitations. Our assumption was that there was no age, sex, or racial/ethnic bias in reporting AHCT to the CIBMTR. It is possible but highly unlikely that such a bias exists in the reporting of data to the CIBMTR and that this could have influenced the STUR across ethnic groups. We note that centers are required to register consecutive patients, and this is audited and monitored by a robust, continuous, performance-improvement process. Second, it is unlikely, given the magnitude of the disparities observed, that systematic underreporting would account for the difference in the STUR, although it could influence the patient differences noted between ethnic groups in terms of those who proceed to transplantation. In addition, our data are based on only those patients who actually proceeded to transplantation, and we cannot comment in this analysis on those patients with MM who did not proceed to AHCT. It is possible, that in areas with a high proportion of Hispanic patients, transplantation centers may not be located at an accessible distance. For instance, for the majority of the time from 2008 through 2013, there was not a local transplantation center for patients in New Mexico or Nevada, where sizable shares of the state populations are Hispanic (48% and 28%, respectively).[23] Eligible patients would have had to travel out of state to undergo transplantation. Previous studies have indicated that such barriers may decrease the receipt transplantation; and this, by itself, may be an important factor in the lower STURs noted among Hispanics.[10] Our strength, however, is in our ability to capture of the majority of patients with MM who underwent an AHCT in the United States.

With clear data demonstrating no differences in outcomes and a clear difference in transplantation utilization by ethnic groups, it is crucial that we now perform additional studies to understand why a disproportionate number of black and Hispanic patients fail to undergo transplantation for MM. It is also important that race and ethnicity should be clearly delineated as factors that do not impact outcomes in terms of proceeding to transplantation. Further education on early referral to transplantation centers for all populations is critical, and efforts should be made to expand community outreach across racial and ethnic groups. Development of strategies to increase access to transplantation across all ethnic groups, with an emphasis on those who are currently underutilizing this modality, is urgently needed.

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CONFLICT OF INTEREST DISCLOSURES

Mohamed A. Kharfan-Dabaja serves on the speakers' bureaus of Incyte Corporation, Seattle Genetics, and Alexion Pharmaceuticals outside the submitted work. Siddhartha Ganguly reports personal fees from Seattle Genetics, Amgen, and Cardinal Health outside the submitted work. Saulius K. Girnius reports personal fees from Celgene and Takeda Pharmaceutical Company outside the submitted work. Tomer M. Mark reports research support from Celgene and Amgen; serves on the advisory boards of Celgene, Takeda Pharmaceutical Company, and Janssen Pharmaceuticals; and serves on the speakers' bureaus of Celgene, Takeda Pharmaceutical Company,

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