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Hispanics have the Lowest Stem Cell Utilization Rate for Autologous Hematopoietic Cell Transplantation for Multiple Myeloma in the United States: a CIBMTR Report

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PRECIS

Race/ethnicity remains a barrier to clinical care. We investigated stem cell utilization rate across race/ethnicity in the United States. Although increasing, STUR remains low and significantly lower among Hispanic followed by non-Hispanic Blacks compared to non-Hispanic Whites. Race/ethnicity does not impact transplant outcomes. Efforts to increase transplant utilization for eligible MM patients, with emphasis on groups underutilizing transplant are warranted.

Accepted Article

Abstract

Background: Race/ethnicity remains an important barrier in clinical care. We investigated differences in autologous hematopoietic cell transplantation (AHCT) utilization in multiple myeloma (MM) and outcomes based on race/ethnicity in the United States.

Methods: The CIBMTR database identified 28,450 patients who underwent AHCT for MM from 2008-2014. Using SEER 18, the incidence of MM was calculated. A stem cell transplant utilization rate (STUR) was derived. Among patients 18-75 years undergoing melphalan-conditioned peripheral cell grafts (N=24,102), we analyzed post-AHCT outcomes.

Results: The STUR increased across all groups from 2008 to 2014. The increase was substantially lower among Hispanics (8.6% to 16.9%) and non-Hispanic Blacks (12.2% to 20.5%) than for non-Hispanic Whites (22.6% to 37.8%). There were 18,046 non-Hispanic Whites, 4123 non-Hispanic Blacks and 1933 Hispanic patients. The Hispanic group was younger ($p < 0.001$). Fewer patients over 60 were transplanted in Hispanic (39%) and non-Hispanic Blacks (42%) vs. non-Hispanic Whites (56%). A Karnofsky score < 90 and Hematopoietic Cell Transplantation-Comorbidity Index > 3 were more common in non-Hispanic Blacks compared to Hispanic and non-Hispanic Whites ($p < 0.001$). More Hispanic (57%) vs. non-Hispanic Blacks (54%) and non-Hispanic Whites (52%) ($p < 0.001$) had stage III disease. More Hispanics (48%) vs. non-Hispanic Blacks (45%) and non-Hispanic Whites (44%) were in \geq very good partial response pre-transplant ($p = 0.005$). Race/Ethnicity did not impact post-AHCT outcomes.

Conclusions: Although increasing, STUR remains low and significantly lower among Hispanic followed by non-Hispanic Blacks compared to non-Hispanic Whites. Race/ethnicity does not impact transplant outcomes. Efforts to increase transplant utilization for eligible MM patients, with emphasis on groups underutilizing transplant are warranted.

Introduction

Recent studies have confirmed the role of upfront autologous hematopoietic cell transplantation (AHCT) in 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 transplant should be considered in patients with symptomatic disease,⁵ studies from the United States (US) suggest that transplant is only used in approximately 30% of MM patients.⁶⁻⁸ Understanding barriers is critical to developing strategies to increase utilization of AHCT as a therapeutic option.

The role of race on the utilization and efficacy of AHCT in patients with MM has been previously studied.⁸⁻¹⁰ Despite a significantly higher incidence of MM in Blacks compared to Whites, these studies have shown lower utilization rates in Blacks. Importantly, studies have also showed that there are no differences in outcomes such as treatment-related mortality and survival after AHCT for MM based on race.^{9,10}

There is little data on the utilization or 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 US. Using the Center for International Blood and Transplant Research (CIBMTR[®]) and Surveillance, Epidemiology and End Results (SEER) databases, we sought to identify differences in transplant utilization and outcomes among self-identified racial and ethnic groups among patients with MM who underwent an AHCT in the US.

Patients and Methods

Data source

The CIBMTR registry is a prospectively maintained transplant database that collects transplant 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, gender, self-identified race/ethnicity, date of diagnosis, graft type, conditioning regimen, post-transplantation disease progression, survival and cause of death and includes all transplants reported to the CIBMTR. Data are collected pre-transplantation, 100 days and 6 months post-transplantation, and annually thereafter until death or last follow up. Between 2008 and 2014, the CIBMTR captured 75-80% of all autologous transplants performed in the US. For the purposes of this study, it was assumed that there was no systematic age, sex, race/ethnicity biases in reporting AHCT to the CIBMTR.

Patients

All US patients registered with the CIBMTR for a first AHCT for MM in 2008-2014 were collected (N=28,450) and used to determine stem cell transplant utilization rate (STUR). Only first transplants were counted. Among these, patients aged 18-75 years who received 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 SEER Program of the US National Cancer Institute. SEER data are derived from registries covering approximately 27.8% of the US population; we used SEER 18 database, which contains patients diagnosed from 2002-2013. Using publicly available software which also provides US population estimates (SEER*Stat, version 8.3.2), we calculated incidence rates per 100,000 persons for the years 2008–2013. SEER provides information according to race and ethnicity yielding the categorization of individuals as Hispanics (irrespective of race), non-Hispanic Blacks (NHB) and non-Hispanic Whites (NHW). For MM patients, SEER provides information on age at diagnosis, gender, prior and subsequent malignancies but not on staging, biologic characteristics (including chromosome abnormalities) or the use of systemic therapy including HCT. We combined MM incidence derived from the SEER program with transplantation activity reported to the Center for International Blood and

Marrow Transplant Research for the period of 2008 to 2013 to assess the impact of disparities in AHCT.

Statistical Analysis

An estimate of transplant rate was calculated. This stem cell transplant utilization rate (STUR) was defined as new AHCT in a given year divided by newly diagnosed number of MM patients for that year. The number of new AHCT each year was calculated as the number of AHCT reported to the CIBMTR divided by the CIBMTR capture rate. Since the estimate of the CIBMTR capture rate during this time was 75-80%, a sensitivity analysis was performed to provide a range to the rate for +/-5% for the CIBMTR AHCT transplant capture rate in each year.

Patient-, disease- and treatment-related factors were compared using the chi-square test for categorical and the Kruskal-Wallis test for continuous variables. Outcomes analyzed included transplant related mortality (TRM), relapse/progression, progression-free survival (PFS) and overall survival (OS). Estimates of outcomes were reported as probabilities with 95% confidence intervals (CI). The probability of OS was calculated with the Kaplan-Meier estimator, with the variance estimated by Greenwood formula. Comparison of survival curves was done with 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 violating 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, a p-value of <0.01 was 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 (Supplemental table). The incidence of MM in the Hispanic and Non-Hispanic White groups remained stable during this period at an incidence rate of 5.6-6.3 per 100,000 for Hispanic and 5.7-6.0 per 100,000 for non-Hispanic White groups. Among the Non-Hispanic Black group, the incidence of MM was nearly double at 12.7-13.7 per 100,000 during this time period. Overall STUR estimate was 19.1 (95% CI: 18.5-19.6) % in 2008 and increased to 30.8 (95% CI: 30.0-31.6)% in 2013. When parsed between the 3 racial/ethnic groups, the STUR estimate increased across all three 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, 12.2 (95% CI:11.4-13.0)% 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 groups.

Table 2 shows the characteristics of 24,102 patients aged 18-75 years undergoing a first AHCT for MM reported to the CIBMTR between 2008 and 2014 who received melphalan conditioning and peripheral hematopoietic cell transplant, with at least 100 days of follow up using CIBMTR registration level data which captured 75-80% of MM AHCT activity in the US during this time period. In this cohort, we identified 18,046 NHW, 1933 H and 4123 non-Hispanic Blacks who underwent transplantation.

There were significant differences in pre-transplant characteristics between groups. The Hispanic group was younger with a median age of 57 (range19-75) years versus non-Hispanic Blacks 58 (20-75) years and non-Hispanic Whites 61 (19-75) years ($p<0.001$). Fewer patients over the age of 60 were transplanted in the Hispanics (39%) and non-Hispanic Blacks (42%) groups versus the non-Hispanic Whites group (56%) ($p< 0.001$). More females underwent transplant in the non-Hispanic Blacks (50%) and Hispanic group (43%) versus the non-Hispanic Whites group (41%) ($p<0.001$). A greater proportion of non-Hispanic Blacks (44%) had lower Karnofsky scores ($< 90\%$) versus Hispanic and non-Hispanic Whites (39% each) ($p<0.001$).

Similarly a higher proportion of non-Hispanic Blacks (38%) and non-Hispanic Whites (34%) had higher hematopoietic cell transplantation-comorbidity index (HCT-CI) of ≥ 3 versus Hispanics (24%) ($p < 0.001$). Advanced stage (Durie-Salmon or ISS Stage III) was more common among the Hispanic (57%) and non-Hispanic Black (54%) groups versus non-Hispanic Whites (52%) ($p < 0.001$). Non-Hispanic Whites had a greater proportion proceeding to transplant < 6 months from diagnosis (30%) versus Hispanic (23%) and non-Hispanic Black patients (21%) ($p < 0.001$). More Hispanic (48%) patients were in a VGPR or better disease status at AHCT compared with non-Hispanic Blacks (45%) and non-Hispanic Whites (44%) ($p < 0.005$).

We then characterized further details of the 1933 Hispanic patients who proceeded to transplant (Table 3). The majority (N=1,590) identified as Hispanic White, 64 as Hispanic Black and 279 as Hispanic Other. There were no differences between these groups noted for age, gender, Karnofsky score, HCT-CI score, time to transplant and pre-transplant staging. There were a higher number of patients with stage III disease in the Hispanic White (59%) versus Hispanic Black (55%) and Hispanic Other (47%) ($p = 0.008$).

Post-transplant outcomes are shown in Table 4. There was no difference seen amongst the different racial and ethnic groups for TRM, PFS or OS (Figure 1). On multivariate analysis (Table 5), race and ethnicity had no influence on survival (Table 5), however older age (61-75 years), male sex, Karnofsky score < 90 , HCT-CI score ≥ 3 , longer interval from diagnosis to transplant (> 12 months), lower melphalan dose for conditioning (140 mg/m^2) and adverse disease status ($< \text{CR}$) pre-transplant adversely affected survival.

Discussion

Multiple myeloma is one 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 US. Multiple studies have shown disparities in

outcomes in MM using SEER data. Pulte, *et al.* showed improvement in age-adjusted 5-year relative survival in MM to increase from 35.6% in 1998-2001 to 44% in 2006-2009.¹¹ However, this increase was greatest for non-Hispanic Whites and excess mortality hazard ratios were observed amongst non-Hispanic Blacks and Hispanics compared to non-Hispanic Whites¹¹ suggesting that ethnic minorities may have not benefited from the advances in MM therapies to similar extent as non-Hispanic Whites patients have. Ailawadhi, *et al.* also showed similar findings using the SEER 17 Registry data.¹²

While 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.^{1-3,13} We conducted this research to better understand disparities in transplant utilization in the US. In this large database study that captures the majority of MM AHCT activity in the US, we make the following observations: 1) STUR in MM has improved significantly from 2008 to 2013; 2) However, despite the increase, overall STUR was only 30.8% in 2013 and lowest among Hispanics followed by non-Hispanic Blacks and highest among non-Hispanic Whites; 3) Hispanic patients who undergo AHCT for MM tend to be younger, fitter and with more advanced disease; 4) Race/ethnicity did not impact post-AHCT MM outcomes.

Despite compelling evidence and NCCN recommendations⁵ that MM patients be evaluated at a stem cell transplant center, transplant utilization remains low at approximately 30.8% in 2013.

Despite an almost doubling of the STUR rate from 8.6 to 16.9 % in Hispanics and a 70% increase in STUR rates in Blacks (12.2 to 20.5%), they remain substantially lower than non-Hispanic Whites which rose from 22.6 to 37.8 % in the same time frame. In addition, the rate increase of transplanted patients from 2008-2013 was far greater in non-Hispanic Whites (15.2 %), versus non-Hispanic Blacks (8.3%) and Hispanic (8.3%) groups. This means that Hispanic patients are transplanted at less than half the rate of non-Hispanic Whites (45%) and non-Hispanic Black patients are transplanted at a just over half the rate (54%) of non-Hispanic

Whites. Others have also shown that non-Hispanic Blacks and Hispanic patients have lower incidence of AHCT in MM.^{6,8} Al-Hamadani, et al. demonstrated that older age, lower levels of education and household income, non-managed 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 in MM.⁶

Joshua, *et al.* has previously showed that transplant, both autologous and allogeneic, is used more frequently in White than in Black individuals to treat leukemia, lymphoma and MM.¹⁰

Our data also show that there is a difference by race/ethnicity in the profile of patients receiving AHCT for MM. Hispanic and non-Hispanic Black patients tend to be younger, with few patients over the age of 60 transplanted among these groups than the non-Hispanic White group. This is particularly poignant in MM, given the median age at diagnosis of MM is 69 years.¹⁴ This finding may also account in part for some of the differences in STUR across race/ethnicities. Hispanic and non-Hispanic Black patients were also more likely to have advanced stage disease at diagnosis and to undergo transplant later from diagnosis than non-Hispanic White patients. This confirms results from a small single center study from Baltimore which showed that among MM patients referred for AHCT, Black patients were younger and often had delayed referrals for AHCT than White patients.¹⁵ We now extend this finding to Hispanic patients as well.

Hispanic patients had a significantly higher percentage with lower comorbidity scores and were more likely to have a better disease status (> VGPR) prior to transplant compared with non-Hispanic Black and non-Hispanic White patients. This suggests that Hispanic patients that undergo transplant tend to be younger, fitter with more advanced but responsive disease and are transplanted later in their disease course than non-Hispanic White patients. Non-Hispanic Black recipients of AHCT are also with a similar profile - younger, with more advanced disease and transplanted later than non-Hispanic White patients. In addition, they were more likely to

have higher comorbidities than non-Hispanic White and Hispanic patients. Fiala, *et al.* showed that the racial disparities between Black and White patients with MM undergoing AHCT are not fully accounted for by age, gender, socioeconomic status, insurance and comorbidities.¹⁶ The Institute of Medicine has also reported that racial and ethnic disparities in healthcare are not entirely explained by the differences in access to care, clinical appropriateness or patient preferences.¹⁷ Studies have also documented differential receipt of technical aspects of care such as tests and therapies and procedures among racial/ ethnic minorities compared with Whites even after the control for insurance status and access to medical care.¹⁸ These data point toward an interplay of many other complex factors such as physician bias, referral bias, cultural beliefs, language barriers, access to transplant center that may affect the utilization of AHCT among different race/ethnic groups. In a single center study, it has been shown that once seen at a transplant center, transplant rates are similar among different ethnic groups.¹⁹ In another setting, namely, the treatment of MM patients in clinical trials in the US, a similar difference has been reported.²⁰

Previous literature, including from the CIBMTR, has shown that post-transplant outcomes are identical regardless of race.^{9,15,21} Our current results extend that literature among ethnic subgroups with identical results. With this in mind and recognizing the differences in STUR, we believe it is time to have a concerted effort to improve STUR among all groups with special emphasis for the low performing ethnicities. NCCN and other national guidelines could address the fact that outcomes for similarly treated patients are comparable across racial and ethnic groups but utilization variable.

Our data have some limitations. Our assumption was that there was no age, sex, race/ethnicity 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 rates across ethnic groups. Notably, centers are required to register consecutive patients and this is

audited and monitored by a robust continuous performance improvement process. Secondly, it is unlikely given the magnitude of the disparities observed that systematic under reporting would account for the difference in STUR rates although it could influence the patient differences noted between ethnic groups in terms of those who proceed to transplant. In addition, our data are based on only those patients who actually proceed to transplant 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 transplant centers may not be located at an accessible distance. For instance, for the majority of the time from 2008-2013 there was not a local transplant center for patients in New Mexico and Nevada where a sizable share of the state population is Hispanic (48% and 28%).²² Eligible patients would have had to travel out of state to get transplant. Previous studies have shown such barriers may decrease utilization of transplant and this by itself may be an important factor in the lower STUR rates noted among Hispanics.¹⁰ Our strength however is in our ability to capture of the majority of MM patients who received an AHCT in the US.

With clear data showing no differences in outcomes and a clear difference in transplant 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 transplant 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 transplant. Further education on early referral to transplant 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 transplant across all ethnic groups with an emphasis on those who are currently underutilizing this modality is urgently needed.

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Manuscript writing: All authors

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Table 1. Stem cell Transplant Utilization Rates in Multiple Myeloma. Incidence rate is age-adjusted and shown per 100,000 persons; STUR rate is shown in percent. Both rates include the 95% confidence intervals in parenthesis.

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

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

Table 4. Univariate outcomes of patients characterized by race/ethnicity (N=24,102)

Table 5. Multivariate analysis of overall survival

Figure 1. Progression-free and Overall survival by race/ethnicity

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Table 1. Stem cell Transplant Utilization Rates in Multiple Myeloma. Incidence rate is age-adjusted and shown per 100,000 persons; STUR rate is shown in percent. Both rates include the 95% confidence intervals in parenthesis.

Year	Hispanic		Non-Hispanic Black		Non-Hispanic White		Overall STUR estimate%
	Incidence	STUR estimate%	Incidence	STUR estimate%	Incidence	STUR estimate%	
2008	5.8 (5.3-6.3)	8.6 (7.9 -9.4)	12.6 (11.7-13.4)	12.2 (11.4 -13.0)	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 (10.9-13.0)	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 (30.0-31.6)

STUR- stem cell utilization rate

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

Variable	Hispanic	Non-Hispanic Black	Non-Hispanic White	P-value
Number of enrolled patients	1933	4123	18046	
Number of centers	111	126	135	
<i><u>Patient-related variables</u></i>				
Median age at transplant, years	57 (19-75)	58 (20-75)	61 (19-75)	<0.001
<45	213 (11)	395 (10)	838 (5)	
45-60	972 (50)	2003 (49)	7164 (40)	
61-75	748 (39)	1725 (42)	10044 (56)	
Gender, Male	1097 (57)	2062 (50)	10693 (59)	<0.001
Karnofsky Score, <90%	750 (39)	1807 (44)	7116 (39)	<0.001
HCT-CI index				<0.001
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)	
<i><u>Disease-related variables</u></i>				
Immunochemical subtype				<0.001
IgG	1055 (55)	2652 (64)	10154 (56)	
IgA	410 (21)	662 (16)	3899 (22)	
Light chain	399 (21)	725 (18)	3469 (19)	
Non-secretory	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)	<0.001
Time from diagnosis to transplant				<0.001
< 6 months	436 (23)	860 (21)	5454 (30)	
6 - 12 months	860 (44)	1839 (45)	7864 (44)	
> 12 months	634 (33)	1420 (34)	4699 (26)	
Missing	3 (<1)	4 (<1)	29 (<1)	
<i><u>Transplant-related variables</u></i>				
Melphalan dose 200 mg/m ²	1636 (85)	3488 (85)	15469 (86)	0.29
Disease Status prior to Transplant				0.005
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-transplant therapy				<0.001
No	1571 (81)	3205 (78)	13426 (74)	
Yes	360 (19)	914 (22)	4585 (25)	
Missing	2 (<1)	4 (<1)	35 (<1)	
Median follow-up of survivors (range), months	36 (1-99)	37 (1-97)	38 (1-98)	

Abbreviations: HCT-CI, hematopoietic cell transplantation-comorbidity index; ISS, International Staging System; DSS, Durie-Salmon Staging; CR, complete response; VGPR, very good partial response; PR, partial response; SD, stable disease

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

Variable	Hispanic White	Hispanic Black	Hispanic Others	P-value
Number of enrolled patients	1590	64	279	
Number of centers	102	32	54	
<u>Patient-related variables</u>				
Median age at transplant, year	57 (19-75)	57 (40-74)	57 (28-74)	0.46
<45	184 (12)	4 (6)	25 (9)	
45-60	793 (50)	32 (50)	147 (53)	
61-75	613 (39)	28 (44)	107 (38)	
Sex, Male	907 (57)	30 (47)	160 (57)	0.27
Karnofsky Score <90%	621 (39)	28 (44)	101 (36)	0.72
HCT-CI index				0.09
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)	0.33
<u>Disease-related variables</u>				
Immunochemical subtype				0.67
IgG	862 (54)	36 (56)	157 (56)	
IgA	340 (21)	11 (17)	59 (21)	
Light chain	332 (21)	15 (23)	52 (19)	
Non-secretory	35 (2)	2 (3)	4 (1)	
Others	21 (1)	0	7 (3)	
ISS/DSS III	934 (59)	35 (55)	131 (47)	0.008
Time from diagnosis to transplant				0.52
< 6 months	369 (23)	12 (19)	55 (20)	
6 - 12 months	711 (45)	26 (41)	123 (44)	
> 12 months	508 (32)	26 (41)	100 (36)	
Missing	2	0	1	
<u>Transplant-related variables</u>				
Melphalan dose 200 mg/m ²	1336 (84)	51 (80)	249 (89)	0.04
Disease status prior transplant				0.98
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-transplant therapy				0.03
No	1294 (81)	60 (94)	217 (78)	
Yes	295 (19)	4 (6)	61 (22)	
Missing	1 (<1)	0	1 (<1)	
Median follow-up of survivors (range), months	37 (1-99)	37 (4-74)	25 (1-82)	

Abbreviations: HCT-CI, hematopoietic cell transplantation-comorbidity index; ISS, International Staging System; DSS, Durie-Salmon Staging; CR, complete response; VGPR, very good partial response; PR, partial response; SD, stable disease

Table 4. Univariate outcomes of patients characterized by race and ethnicity (N=24,102)

Outcomes	Hispanic (N = 1933)		Non-Hispanic Black (N = 4123)		Non-Hispanic White (N = 18046)		p-value
	N	Prob (95% CI)	N	Prob (95% CI)	N	Prob (95% CI)	
NRM	1926		4104		18006		0.36‡
100 day		0.6 (0.3-1)%		0.6 (0.4-0.9)%		0.9 (0.7-1)%	0.15
1-year		2 (2-3)%		3 (2-3)%		3 (2-3)%	0.70
PFS	1926		4104		18006		1.0‡
1-year		82 (80-84)%		82 (81-83)%		83 (82-83)%	0.30
2-year		66 (64-68)%		66 (64-67)%		66 (65-67)%	0.93
3-year		54 (51-56)%		54 (52-55)%		53 (52-54)%	0.84
OS	1932		4120		18030		0.13‡
1-year		94 (93-95)%		94 (94-95)%		94 (93-94)%	0.26
2-year		86 (85-88)%		86 (85-87)%		86 (85-86)%	0.72
3-year		80 (77-82)%		79 (77-80)%		77 (77-78)%	0.05

Abbreviations: NRM, non-relapse mortality; PFS, progression-free survival; OS, overall survival

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Table 5. Multivariate analysis of overall survival

Effect	Hazard Ratio (95% CI)	p-value
Main Effect		0.08
Hispanic	1	
Non-Hispanic Black	0.99 (0.89-1.11)	0.2
Non-Hispanic White	1.07 (0.97-1.18)	0.9
Age		<.0001
<45	1	
45-60	1.15 (1.02-1.30)	0.02
61-75	1.33(1.18-1.50)	<.0001
Gender		<.0001
Male	1	
Female	0.87 (0.823-0.92)	
Karnofsky score		<.0001
≥90%	1	
<90%	1.23 (1.19-1.32)	
Missing	1.14 (1.01-1.29)	
HCT-CI		<.0001
No comorbidity	1	
1-2	1.04 (0.97-1.11)	0.26
≥3	1.21 (1.13-1.29)	<.0001
Missing	0.87 (0.79-0.96)	0.006
Stage at diagnosis		<.0001
<III	1	
III	1.46 (1.39-1.54)	<.0001
Missing	1.17 (1.02-1.34)	0.02
Time from diagnosis to transplant		<.0001
<6 months	1	
6-12 months	1.08 (1.01-1.15)	0.03
>12 months	1.44 (1.34-1.54)	<.0001
Missing	2.13 (1.28-3.55)	0.004
Melphalan dose		<.0001
140 mg/m ²	1	
200 mg/m ²	0.85 (0.80-0.91)	<.0001
Missing	0.41 (0.06-2.93)	0.4
Disease status at transplant		<.0001
sCR/CR	1	
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)	0.2

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

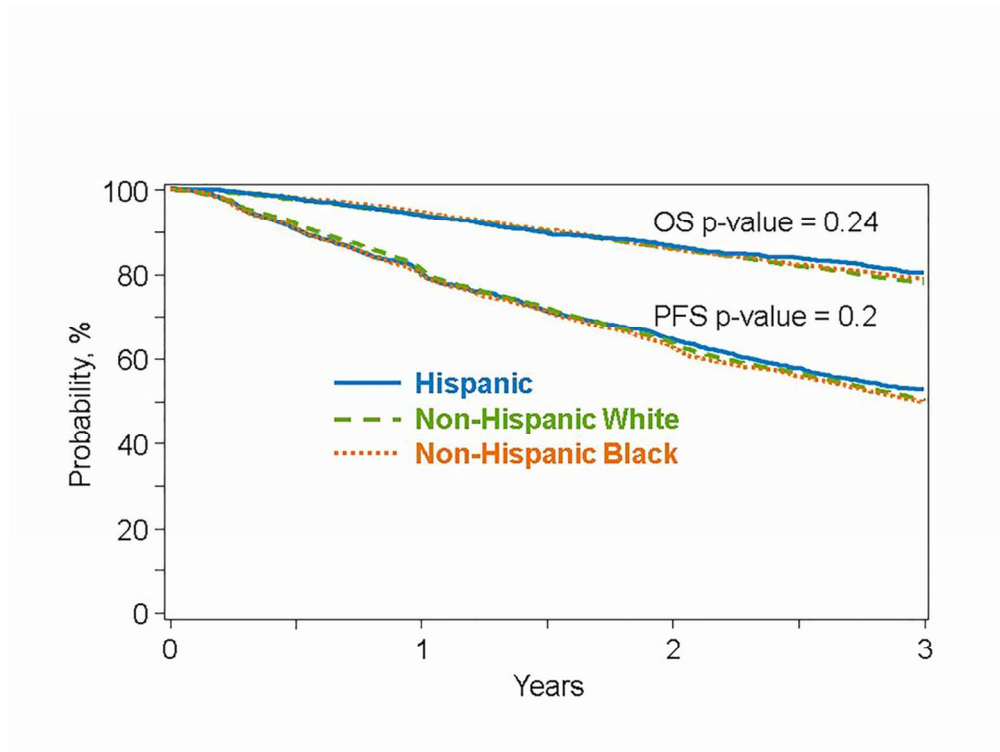


Figure 1. Progression-free and overall survival after autologous hematopoietic cell transplantation by race/ethnicity

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Supplementary table 1: STUR calculation table with raw data:

Years	CIBMTR AUTO HCT transplant number				SEER MM incidence rate‡			US population			STUR(%)		
	H	NHW	NHB*	Adjusted rate†	H	NHW	NHB*	H	NHW	NHB*	H	NHW	NHB*
2008	175	1876	425	0.75	5.8 (5.3-6.3)	5.7 (5.5-5.9)	12.6 (11.7-13.4)	47,793,785	197,183,535	37,171,750	8.6 (7.9-9.4)	22.6 (21.8-23.9)	12.2 (11.4-13.0)
2009	223	2373	513	0.8	5.9 (5.4-6.4)	5.7 (5.5-5.9)	12.9 (12.1-13.8)	49,327,489	197,274,549	37,681,544	9.8 (9.0-10.7)	26.6 (25.7-27.5)	13.2 (12.4-14)
2010	288	2779	619	0.8	6.0 (5.5-6.5)	6.0 (5.8-6.2)	12.9 (12.2-13.8)	50,810,213	197,380,184	38,007,630	11.9 (10.9-13.0)	29.4 (28.4-30.4)	15.7 (14.8-16.8)
2011	301	3146	740	0.8	6.3 (5.9-6.9)	5.9 (5.7-6.1)	13.3 (12.5-14.1)	51,953,707	197,497,845	38,361,614	11.4 (10.6-12.4)	34 (32.9-35.1)	18.2 (17.1-19.3)
2012	372	3345	793	0.8	6.2 (5.7-6.7)	6.0 (5.8-6.2)	13.7 (12.9-14.5)	53,074,304	197,668,557	38,725,652	14.2 (13.1-15.4)	35.4 (34.3-36.6)	19 (18-20.2)
2013	410	3358	838	0.8	5.6 (5.2-6.1)	5.8 (5.6-6.0)	13.3 (12.5-14.1)	54,203,686	197,741,352	39,076,459	16.9 (15.6-18.3)	37.8 (35.5-38)	20.5 (19.4-21.8)

* In SEER database, only incidence of Black is provided. We assume the Non-Hispanic black rate is the same as black rate.

† CIBMTR AUTO HCT capture rate

‡ MM Incidence rate: 1 in 100,000

**STUR = (# of AUTO transplant each year)/(# of incidence each year). In which, # of AUTO transplant each year = # AUTO in CIBMTR/adjusted rate; # of incidence each year = SEER incidence rate * US population;

Supplementary table 2: STUR calculation sensitive analysis:

Years	H	NHW	NHB*	H	NHW	NHB*	H	NHW	NHB*	H	NHW	NHB*
	CIBMTR AUTO capture rate +5%			CIBMTR AUTO capture rate +10%			CIBMTR AUTO capture rate +15%			CIBMTR AUTO capture rate +20%		
2008	7.9 (7.4-8.8)	21.0 (20.3-21.8)	11.3 (10.7-12.2)	7.4 (7.0-8.3)	19.8 (19.1-20.5)	10.6 (10.1-11.5)	7.0 (6.6-7.9)	18.7 (18.1-19.3)	10.0 (9.5-10.8)	6.6 (6.2-7.4)	17.7 (17.1-18.3)	9.5 (9.0-10.3)
2009	9.1 (8.5-10.0)	24.8 (24.0-25.7)	12.5 (11.7-13.2)	8.6 (8.0-9.5)	23.4 (22.6-24.2)	11.8 (11.0-12.5)	8.2 (7.6-9.0)	22.2 (21.5-23.0)	11.1 (10.4-11.8)	7.8 (7.2-8.6)	21.1 (20.4-21.8)	10.6 (9.9-11.2)
2010	11.3 (10.3-12.2)	28.8 (26.8-28.6)	14.7 (14.0-15.8)	10.7 (9.7-11.5)	27.2 (25.3-27.0)	13.9 (13.2-14.9)	10.1 (9.2-10.9)	25.7 (24.0-25.6)	13.2 (12.5-14.1)	9.6 (8.7-10.4)	24.5 (22.8-24.3)	12.5 (11.8-13.4)
2011	11.5 (10-11.7)	32.3 (31.0-33.0)	17.2 (16.1-18.2)	10.9 (9.4-11.0)	30.5 (29.2-31.2)	16.2 (15.2-17.2)	10.3 (9.0-10.4)	28.9 (27.7-29.6)	15.4 (14.4-16.3)	9.8 (8.5-9.9)	27.4 (26.3-28.1)	14.6 (13.7-15.4)
2012	14.0 (12.4-14.4)	34.0 (32.3-34.4)	18.0 (16.7-18.7)	13.2 (11.7-13.6)	32.1 (30.5-32.5)	17.0 (15.7-17.7)	12.5 (11.0-12.9)	30.4 (28.9-30.8)	16.1 (14.9-16.7)	11.9 (10.5-12.3)	28.9 (27.4-29.3)	15.3 (14.2-15.9)
2013	15.1 (14.6-17.2)	33.8 (33.3-35.6)	18.6 (18.0-20.1)	14.3 (13.8-16.2)	31.9 (31.5-33.6)	17.6 (17.0-19)	13.5 (13.1-15.4)	30.2 (29.8-31.9)	16.7 (16.0-18.0)	12.8 (12.4-14.6)	28.7 (28.3-30.3)	15.8 (15.2-17.1)
	CIBMTR AUTO capture rate -5%			CIBMTR AUTO capture rate -10%			CIBMTR AUTO capture rate -15%			CIBMTR AUTO capture rate -20%		
2008	9.0 (8.4-10.1)	24.0 (23.2-24.9)	12.9 (12.2-14.9)	9.7 (9.1-10.9)	25.9 (25.0-26.8)	13.9 (13.2-15.0)	10.5 (9.8-11.8)	28.1 (27.1-29.0)	15.0 (14.3-16.2)	11.4 (10.7-12.9)	30.6 (29.5-31.6)	16.4 (5.6-17.7)
2009	10.4 (9.6-11.4)	28.1 (27.2-29.1)	14.1 (13.2-15.0)	11.1 (10.3-12.3)	30.1 (29.1-31.2)	15.1 (14.1-16.0)	12.0 (11.1-13.2)	32.4 (31.4-33.6)	16.3 (15.2-17.3)	13.0 (12.0-14.3)	35.1 (34.0-36.4)	17.6 (16.5-18.7)
2010	12.8 (11.7-13.8)	32.6 (30.3-32.4)	16.7 (15.8-17.9)	13.7 (12.5-14.8)	34.9 (32.5-34.7)	17.9 (16.9-19.2)	14.8 (13.5-15.9)	37.6 (35.0-37.4)	19.2 (18.2-20.6)	16.0 (14.6-17.3)	40.8 (37.9-40.5)	20.8 (19.7-22.3)
2011	13.1 (11.3-13.2)	36.6 (35.1-37.5)	19.5 (18.3-20.6)	14.0 (12.1-14.2)	39.2 (37.6-40.2)	20.9 (19.6-22.1)	15.1 (13.0-15.3)	42.2 (40.5-43.3)	22.5 (21.1-23.7)	16.4 (14.1-16.5)	45.7 (43.8-46.9)	24.4 (22.8-25.7)
2012	15.8 (14.0-16.4)	38.5 (36.6-39.0)	20.4 (18.9-21.2)	17.0 (15.0-17.5)	41.2 (39.2-41.8)	21.9 (20.2-22.7)	18.3 (16.2-18.9)	44.4 (42.2-45.0)	23.6 (21.8-24.5)	19.8 (17.5-20.5)	48.1 (45.7-48.8)	25.5 (23.6-26.5)
2013	17.1 (16.6-19.4)	38.3 (37.8-40.4)	21.1 (20.3-22.8)	18.3 (17.8-20.8)	41.0 (40.5-43.3)	22.6 (21.8-24.4)	19.8 (19.1-22.4)	44.1 (43.6-46.6)	24.4 (23.4-26.3)	21.4 (20.7-24.3)	47.8 (47.2-50.5)	26.4 (25.4-28.5)

* In SEER database, only incidence of Black is provided. We assume the Non-Hispanic black rate is the same as black rate.

† CIBMTR AUTO HCT capture rate

‡ MM Incidence rate: 1 in 100,000

**STUR = (# of AUTO transplant each year)/(# of incidence each year). In which, # of AUTO transplant each year = # AUTO in CIBMTR/adjusted rate; # of incidence each year = SEER incidence rate * US population;