HHS Public Access

Author manuscript

Bone Marrow Transplant. Author manuscript; available in PMC 2015 July 13.

Published in final edited form as:

Bone Marrow Transplant. 2013 March ; 48(3): 346–350. doi:10.1038/bmt.2012.150.

Race/ethnicity affects the probability of finding an HLA-A, -B, -C and -DRB1 allele-matched unrelated donor and likelihood of subsequent transplant utilization

J Pidala[1,2], **J Kim**[2,3], **M Schell**[2,3], **SJ Lee**[4], **R Hillgruber**[1], **V Nye**[1], **E Ayala**[1,2], **M Alsina**[1,2], **B Betts**[1,2], **R Bookout**[1,2], **HF Fernandez**[1,2], **T Field**[1,2], **FL Locke**[1,2], **T Nishihori**[1,2], **JL Ochoa**[1,2], **L Perez**[1,2], **J Perkins**[1,2], **J Shapiro**[1,2], **C Tate**[1,2], **M Tomblyn**[1,2], and **C Anasetti**[1,2]

[1]Blood and Marrow Transplantation, Moffitt Cancer Center, Tampa, FL, USA

[2]Oncologic Sciences, University of South Florida, Tampa, FL, USA

[3]Biostatistics, Moffitt Cancer Center, Tampa, FL, USA

[4]Clinical Research Division, Fred Hutchinson Cancer Research Center, Seattle, WA, USA

Abstract

Factors relevant to finding a suitable unrelated donor and barriers to effective transplant utilization are incompletely understood. Among a consecutive series of unrelated searches (n = 531), an 8/8 HLA-A, -B, -C and -DRB1-matched unrelated donor was available for 289 (54%) patients, 7/8 for 159 (30%) and no donor for 83 (16%). Patients of Caucasian race ($P < 0.0001$) were more likely to find a donor. Younger age ($P = 0.01$), Caucasian race ($P = 0.03$), lower CIBMTR (Center for International Blood and Marrow Transplantation Research) risk ($P = 0.005$), and 8/8 HLA matching ($P = 0.005$) were associated with higher odds of reaching hematopoietic cell transplantation (HCT). In a univariate analysis of OS, finding a donor was associated with hazard ratio (HR) of 0.85 (95% CI 0.63–1.2), $P = 0.31$. Karnofsky performance status (KPS) accounted for interaction between having a donor and survival. Patients with KPS 90–100 and a donor had significantly reduced hazard for death (HR 0.59, 95% CI 0.38–0.90, $P = 0.02$). These data provide estimates of the probability to find an unrelated donor in the era of high-resolution HLA typing, and identify potentially modifiable barriers to reaching HCT. Further efforts are needed to enhance effective donor identification and transplant utilization, particularly in non-Caucasian ethnic groups.

Keywords

unrelated donor; allogeneic hematopoietic cell transplantation; race/ethnicity; HLA; donor vs no donor analysis

Correspondence: Dr J Pidala, Blood and Marrow Transplantation, Moffitt Cancer Center, 12902 Magnolia Drive, FOB 3308, Tampa, FL 33612, USA, joseph.pidala@moffitt.org.

Conflict of Interest: The authors declare no conflict of interest.

Author Contributions: Joseph Pidala—designed research, performed analyses and wrote the paper. JK, MS—performed statistical analyses and contributed to writing of the manuscript. SJL, RH, VN, EA, MA, BB, RB, HFF, TF, FLL, TN, JLO, LP, JP, JS, CT, MT—all contributed to critical analysis and writing of the manuscript. CA—contributed to the study design, analysis and writing of the manuscript.

Introduction

Although allogeneic hematopoietic cell transplantation (HCT) offers potentially curative therapy for hematologic disorders, the majority of HCT candidates will not have a HLA identical sibling. Therefore, unrelated volunteer donors serve a vital role in allowing successful HCT.[1] Identification of a suitable unrelated donor differs according to race and ethnicity: NMDP estimates suggest that a 7–8/8 allele-matched adult unrelated donor may be identified for ∼90% of US or European Caucasians, >70% of Asian or Hispanic, and 60% of those of African ancestry (Dennis Confer, personal communication). As the degree of HLA mismatching increases, the success of unrelated donor HCT falls,[2] but may still be superior to survival offered by non-transplant therapy.

Little is known about the true success of identifying a suitable unrelated donor because so many potential factors may have a role in the process. Distinguishing the biologic determinants of survival such as disease risk and treatment tolerance from the non-biologic determinants such as availability of an allogeneic donor is very complicated. Although the unrelated donor registries keep minimal statistics about the number of formal searches initiated and their ultimate outcome, they lack the detailed patient information about disease risk, disease status and other factors that are critical to understand the complete clinical context in which the search was started.

Using the detailed data available from a single institution, we sought to describe the determinants of a successful unrelated donor search and to explore the contribution of donor identification vs other patient characteristics to successful treatment outcome.

Materials and Methods

All unrelated donor searches initiated between March 2006 and December 2009 by the Blood and Marrow Transplantation Program at the Moffitt Cancer Center were included. Conduct of this analysis was performed with the approval of the University of South Florida Institutional Review Board. All patients had high resolution typing performed by DNA sequencing and had unrelated donor searches facilitated by dedicated National Marrow Donor Program (Minneapolis, MN, USA) histocompatibility specialists. Those patients with a fully HLA-A, -B, -C, and -DRB1 (8/8) or 7/8 (one mismatch at any of these loci) matched unrelated donor according to these high resolution sequencing methods were considered to have a suitable unrelated donor, and were assigned ‘donor’ status for this analysis. Those with < 7/8 matched unrelated donor were considered ‘no donor’. HLA-DP and -DQ loci were not considered for determination of donor vs no donor status. Initiation of unrelated donor searches was at the discretion of the treating physician but would generally be requested once the determination that allogeneic transplantation was recommended but no appropriate related donor was identified.

Data regarding the search process were routinely collected and included date of unrelated donor search initiation, date of identification of a suitable unrelated donor (defined as the date when confirmatory typing on a freshly drawn donor sample identified the first suitable donor), date such donor was cleared to donate and date HCT was performed. Patient

characteristics included age, gender, socio-economic status (derived from the zip code of primary residence using Zip Code Deluxe software), race and ethnicity (White, non-Hispanic; Hispanic; Black/African American; Asian; Native Hawaiian/Pacific Islander; American Indian/Alaskan Native or other); disease condition requiring transplantation, remission status, disease risk category according to Center for International Blood and Marrow Transplantation Research (CIBMTR) criteria, Karnofsky performance status (KPS), ABO blood type and CMV serologic status.

Treatment data were also collected from medical records. For those who had a suitable unrelated donor identified, but did not undergo HCT, the primary reason was coded according to standard criteria per the National Marrow Donor Program. For those who did not have a suitable donor identified, actual treatment delivered (for example, chemotherapy, auto-HCT, immunotherapy, umbilical cord blood transplant) was recorded. Vital status was confirmed using internal records, the social security death index, cancer registry or by contacting primary referring physicians.

Statistical methods

Appropriate statistics (median, range) were utilized to summarize descriptive data. The proportion of those with a suitable unrelated donor was compared across relevant groups, including recipient age, disease condition and race/ethnicity with the Fisher exact test.

To determine the odds ratio for reaching transplant among those with a suitable unrelated donor, we performed logistic regression analysis examining patient socio-demographic and disease variables. All variables with P-value < 0.25 were incorporated into a multivariable model. Backward elimination method was utilized with a P-out value of 0.15.

To explore whether donor availability *per se* was associated with survival, we analyzed survival from date of search initiation to death or last follow-up using a time-dependent Cox regression model, in which donor status was treated as a time-dependent covariate. This analysis adjusts for differing lengths of time to identify unrelated donors for individual patients. In a separate approach, we performed a landmark survival analysis using Cox regression, in which the survival time was calculated from a landmark that contained 95% of the values for time from search initiation to time of identification of a 7/8 or 8/8 matched unrelated donor. In this analysis, patients who die before reaching the landmark are excluded, regardless of whether an unrelated donor was identified for them. Finally, we explored different ways of handling patients who proceeded to HCT using umbilical cord blood, by either (a) including them in the no donor group; or (b) using a time varying covariate to indicate umbilical cord HCT. Additional analyses were performed to examine the impact of degree of HLA matching (7/8 vs 8/8 among the donor group). Finally, we performed descriptive analyses according to receipt of intended therapy (HCT vs no HCT) among the donor group. Additional covariates considered for each analysis included patient age at search initiation, gender, socio-economic status, race/ethnicity, disease diagnosis, CIBMTR risk category, KPS and CMV serostatus. Variables with a P-value of 0.25 or less in univariable analysis were incorporated into the multivariable model. The backward elimination method was used to build the final multivariable model, with P-out value of 0.15.

Results

Patient characteristics

From March 2006 to December 2009, a total of 531 unrelated donor searches were conducted at the Moffitt Cancer Center. Of these, 448 had a suitable unrelated donor identified, matched at 8/8 for 289 (54%) patients and 7/8 for 159 (30%), and 83 (16%) had no suitable adult unrelated donor identified. Baseline patient socio-demographic and disease variables are summarized in Table 1. The median time from search initiation to the time of first suitable donor identified was 21 days (range 7–1026), with only 5% taking longer than 59 days.

Factors associated with identification of a suitable unrelated donor

Both disease diagnosis and race/ethnicity were significantly associated with the likelihood of finding a 7/8 or 8/8 matched unrelated donor. Such a donor was identified in 70% of ALL cases, 89% of AML, 88% of MDS (myelodysplastic syndrome)/MPD (myeloproliferative disorder), 83% of MM (multiple myeloma)/NHL (non-Hodgkin lymphoma)/HD (Hodgkin lymphoma)/CLL and 77% of SAA (severe aplastic anemia)/PNH (paroxysmal nocturnal hemoglobinuria), $P = 0.01$. A 7/8 or 8/8 donor was identified in 354/395 (90%) of White/non-Hispanic patients, 59/78 (76%) of Hispanics, 34/55 (62%) of Black/African Americans and 1/3 (33%) of Asians ($P < 0.0001$). No other clinical characteristics were significantly associated with finding a suitable unrelated donor.

Factors associated with undergoing transplantation

Among the 448 who were able to identify a suitable (8/8 or 7/8) unrelated donor, 239 (53%) underwent HCT. In univariable analysis, age, race/ethnicity, CIBMTR risk category, and degree of HLA match were significantly associated with HCT. In multivariable analysis, increasing age (odds ratio (OR) 0.81 per 10 year increase, 95% CI 0.70–0.95, $P = 0.01$) and greater CIBMTR risk (high vs others, OR 0.57, 95% CI 0.38–0.84, $P = 0.005$) were associated with lower odds of undergoing HCT despite identification of an unrelated donor. Conversely, Caucasian vs other race/ethnicity (OR 1.8, 95% CI 1.1–2.9, $P = 0.03$) and 8/8 vs 7/8 match (OR 1.8, 95% CI 1.2–2.8, $P = 0.005$) were associated with increased odds of proceeding to HCT. KPS was not significantly associated with undergoing HCT.

Availability of a donor and survival

Median follow-up time for surviving patients was 24 months (range 1–52) in the donor group, and 23 months (range 5–52) in the no donor group. In univariable analysis, having a donor identified was associated with a hazard ratio (HR) of 0.87, 95% CI 0.64–1.20, $P = 0.38$ compared with the group without a donor. Age at search initiation, CIBMTR risk category, recipient CMV serostatus, disease type and KPS were selected for inclusion in the multivariable model based on univariable results. A significant interaction was detected between donor status and KPS ($P = 0.01$): better KPS accentuated the prognostic significance of donor availability. Patient, disease and transplantation variables according to KPS groups are presented in Table 2. In a multivariable model accounting for the interaction between donor status and KPS (Table 3), there was a survival advantage for those with KPS

90–100 who had a donor compared with those with KPS 90–100 who had no donor (HR 0.59, 95% CI 0.38–0.90, $P = 0.02$). In those with KPS≤80, availability of a donor was not associated with better survival (HR 0.91, 95% CI 0.59–1.4, $P = 0.67$). In these analyses, patients with an identified donor were included in the donor group, regardless of whether they actually underwent HCT. The causes of death according to donor status are shown in Table 4. Analyses performed according to degree of HLA match did not demonstrate significant impact on outcome.

Reasons for not proceeding to unrelated transplantation after an unrelated donor is identified

Fifty-three percent (239/448) of those patients who had a donor identified actually underwent HCT. Reasons for not proceeding to HCT included: disease progression ($n = 74$, 35%), patient decided against HCT ($n = 21$, 10%), medically ineligible ($n = 15$, 7%), patient died before HCT ($n = 13$, 6%), physician chose alternative therapy ($n = 13$, 6%), waited for better match ($n = 12$, 6%), stable disease ($n = 11$, 5%), lost to follow-up ($n = 9$, 4%), other reasons ($n = 5$, 2%), no caregiver ($n = 3$, 1%), no insurance coverage ($n = 3$, 1%), psychiatric co-morbidity ($n = 3$, 1%), hospice care ($n = 1$) and unknown ($n = 26$, 12%). Of the 209 patients who had a suitable donor identified but did not proceed to HCT, donor availability (unavailable, $n = 9$; temporarily unavailable, $n = 2$) was infrequently identified as a barrier. Of those in the no donor group, 14 underwent double umbilical cord blood transplant (dUCBT). Other identified therapies delivered in the no donor group included: no treatment ($n = 2$), immunotherapy ($n = 2$), autologous transplant ($n = 2$), chemotherapy ($n = 1$) and 6/8-mismatched unrelated donor HCT ($n = 1$). In the 22 (27%) remaining cases, specific therapy delivered was not identified.

Survival analysis according to treatment received

In a descriptive analysis, we examined outcomes according to treatment received. Analysis comparing HCT vs no HCT in the donor group vs no donor (reference group) demonstrated that those who received the intended HCT had significantly reduced hazard for death in both the time-dependent model (HR 0.64, 95% CI 0.46–0.89, $P = 0.009$) and the landmark model (HR 0.68, 95% CI 0.47–0.97, $P = 0.036$), adjusting for other clinical covariates.

To account for the impact of dUCBT in the no donor group on outcome, we constructed a Cox model with time-varying covariates, in which donor, dUCBT and no donor (who did not receive dUCBT) were treated as mutually exclusive time-dependent variables. This analysis demonstrated a significantly reduced hazard for death for the donor vs no donor (no dUCBT) group, HR 0.57, 95% CI 0.43–0.76, $P = 0.0001$.

Discussion

The use of adult volunteer unrelated donors to facilitate allogeneic HCT has provided major opportunities for those patients without a matched sibling donor, and unrelated donor transplantation now exceeds the rate of related donor HCT. Although there is a lack of rigorous data comparing unrelated donor HCT to non-transplant therapy, extensive observational data support that many patients can achieve prolonged condition-free survival

following unrelated donor HCT. However, challenges in finding a suitably matched unrelated donor and barriers to effectively reaching HCT once a donor is identified may limit access to this potentially curative therapy. Thus, there is great need to understand modifiable factors that limit access to unrelated donor HCT.

This analysis demonstrates that identification of a suitably matched unrelated donor by high-resolution HLA typing methods is dependent upon race/ethnicity. This disparity is likely driven both by increased heterogeneity within these ethnic populations, as well as by relative under-representation of these groups in the available unrelated donor registries. Several factors may help address this problem: Increased representation of such ethnic groups within existing unrelated donor registries will increase the likelihood of finding a suitable donor. This is particularly important, as the greatest contribution comes from donors within shared ethnic groups. As certain ethnic groups, particularly African American, Hispanic and Native Americans, will have a relatively greater likelihood of finding a donor outside of their immediate ethnic group in comparison with Caucasians, ongoing increase in general registry inventory may also facilitate donor identification. We acknowledge that, although representative of usual patients seen in our transplant center, the series has poor representation of Asian and Pacific Islander and Native American ethnic groups. As well, although this analysis focused on adult unrelated donor utilization, alternative donor sources including umbilical cord blood and haploidentical transplantation represent important opportunities for donor identification and access to HCT.[3] Improved HCT technology in these alternative donor settings aimed at reducing GVHD and HCT-related mortality,[4–7] shortening time to engraftment,[8–11] and transplantation of umbilical cord blood products of sufficient cell dose and HLA match[12,13] will contribute to their success.[14,15]

This analysis also provides important insight into barriers to reaching unrelated donor HCT once a suitable donor has been identified. First, increasing age was associated with decreased odds of reaching HCT. An expanding body of literature supports the notion that age alone should not be prohibitive, and that reduced intensity conditioning may limit HCT mortality. Although assessment of comorbidity may help better discern risk,[16] more sophisticated selection of appropriate older HCT candidates may be achieved through assessment of frailty and anticipated treatment toxicity.[17,18] Second, greater CIBMTR disease risk was associated with decreased odds of reaching HCT, and progression of disease was the leading reason for not proceeding with HCT. These data speak to the need to reduce the time from HCT consultation and subsequent donor identification to time of HCT. While the optimal search strategy is not known, more aggressive search strategies (for example, simultaneous search for adult unrelated donors and umbilical cord blood units) may offer a risk-adapted approach for patients with high risk of disease progression and/or poor *a priori* likelihood of finding a suitably matched adult unrelated donor. Next, those with 7/8 match were less likely to reach HCT than those with 8/8 match. While many factors may be at work here, this is likely informed by both patient and physician perception of risk associated with mismatched unrelated donor HCT. While large registry analyses have demonstrated increased risk for mortality with single antigen- or allele-level HLA mismatch,[2] certain patients—particularly those of non-Caucasian ethnic groups—are unlikely to find a perfectly matched unrelated donor. Thus, not pursuing HCT under these

conditions may result in missed opportunities for HCT altogether. Finally, non-Caucasian ethnic groups were less likely to proceed to HCT. Several factors are likely at work here. Donor availability, in particular, is a notable problem in those ethnic groups with already low donor match rates; this drops from 57% in Caucasians to 27% in African Americans. Given the small number of cases of donor unavailability identified in our series, we are unable to comment further on the relationship between donor availability and race/ethnicity of the patient. Registry modeling performed by the NMDP and CIBMTR (Dennis Confer, personal communication) has shown that increased donor availability represents one of the mechanisms with greatest likelihood for improved effective match rates leading to HCT.

Finally, these observational data support the efficacy of unrelated donor HCT among patients with good performance status. Given the lack of comparative effectiveness data and selection bias at work in existing reports of unrelated donor HCT outcomes, we performed a donor vs no donor analysis to discern the impact of donor status on survival outcome. The survival benefit suggested by this analysis further supports the importance of finding a suitable donor in a timely manner and addressing modifiable barriers to reaching HCT. Other major determinants of survival outcome in this analysis including age, disease and CIBMTR risk category are consistent with previously published analyses. In contrast to previously reported analyses,[19–22] we could not demonstrate significant association between race/ethnicity or socio-economic status and transplant outcome. Performing a donor vs no donor (intention-to-treat) comparison in the setting of unrelated donor HCT represents an adaptation from methods utilized in sibling donor HCT literature where a ‘genetic randomization’ represents the best approximation of a true randomized comparison.[23] We recognize that identification of HLA-matched siblings is relatively straightforward, quick and performed early in the disease course before significant loss of subjects due to disease progression or treatment toxicity. However, the issue of low compliance with the intended therapy plagues both settings. Although rigorous statistical approaches can somewhat mitigate these concerns, we acknowledge that these remain observational data. Only a true randomized study with close to 100% expeditious unrelated donor identification could definitively answer the question of the value of unrelated donor transplantation. Given the current landscape and size, and diversity of the unrelated registries, this study is not feasible for multiple reasons.

In conclusion, we confirmed that race and ethnicity remain major barriers not only to identification of suitable unrelated donors but also to proceeding to HCT once a donor is identified. Disease progression was the major reason why patients with identified donors did not undergo HCT, but even including the outcomes of these patients in the ‘donor’ group, we still observed a benefit for the group for whom a donor could be identified, particularly those with better performance status. Our data are consistent with the expectation that—if suitable unrelated donors could be more expeditiously identified—patient outcomes would improve, particularly for racial and ethnic minorities and patients with better performance status.

References

1. Karanes C, Nelson GO, Chitphakdithai P, Agura E, Ballen KK, Bolan CD, et al. Twenty years of unrelated donor hematopoietic cell transplantation for adult recipients facilitated by the National Marrow Donor Program. Biol Blood Marrow Transplant. 2008; 14(9 Suppl):8–15. [PubMed: 18721775]
2. Lee SJ, Klein J, Haagenson M, Baxter-Lowe LA, Confer DL, Eapen M, et al. High-resolution donor-recipient HLA matching contributes to the success of unrelated donor marrow transplantation. Blood. 2007; 110:4576–4583. [PubMed: 17785583]
3. Barker JN, Byam CE, Kernan NA, Lee SS, Hawke RM, Doshi KA, et al. Availability of cord blood extends allogeneic hematopoietic stem cell transplant access to racial and ethnic minorities. Biol Blood Marrow Transplant. 2010; 16:1541–1548. [PubMed: 20800103]
4. Brunstein CG, Fuchs EJ, Carter SL, Karanes C, Costa LJ, Wu J, et al. Alternative donor transplantation after reduced intensity conditioning: results of parallel phase 2 trials using partially HLA-mismatched related bone marrow or unrelated double umbilical cord blood grafts. Blood. 2011; 118:282–288. [PubMed: 21527516]
5. Luznik L, O'Donnell PV, Symons HJ, Chen AR, Leffell MS, Zahurak M, et al. HLA-haploidentical bone marrow transplantation for hematologic malignancies using nonmyeloablative conditioning and high-dose, posttransplantation cyclophosphamide. Biol Blood Marrow Transplant. 2008; 14:641–650. [PubMed: 18489989]
6. Brunstein CG, Miller JS, Cao Q, McKenna DH, Hippen KL, Curtsinger J, et al. Infusion of ex vivo expanded T regulatory cells in adults transplanted with umbilical cord blood: safety profile and detection kinetics. Blood. 2011; 117:1061–1070. [PubMed: 20952687]
7. Di Ianni M, Falzetti F, Carotti A, Terenzi A, Del Papa B, Perruccio K, et al. Immunoselection and clinical use of T regulatory cells in HLA-haploidentical stem cell transplantation. Best Pract Res Clin Haematol. 2011; 24:459–466. [PubMed: 21925099]
8. Liu H, Rich ES, Godley L, Odenike O, Joseph L, Marino S, et al. Reduced-intensity conditioning with combined haploidentical and cord blood transplantation results in rapid engraftment, low GVHD, and durable remissions. Blood. 2011; 118:6438–6445. [PubMed: 21976674]
9. Delaney C, Heimfeld S, Brashem-Stein C, Voorhies H, Manger RL, Bernstein ID. Notch-mediated expansion of human cord blood progenitor cells capable of rapid myeloid reconstitution. Nat Med. 2010; 16:232–236. [PubMed: 20081862]
10. Delaney M, Cutler CS, Haspel RL, Yeap BY, McAfee SL, Dey BR, et al. High-resolution HLA matching in double-umbilical-cord-blood reduced-intensity transplantation in adults. Transfusion. 2009; 49:995–1002. [PubMed: 19159415]
11. Frassoni F, Gualandi F, Podesta M, Raiola AM, Ibatici A, Piaggio G, et al. Direct intrabone transplant of unrelated cord-blood cells in acute leukaemia: a phase I/II study. Lancet Oncol. 2008; 9:831–839. [PubMed: 18693069]
12. Barker JN, Scaradavou A, Stevens CE. Combined effect of total nucleated cell dose and HLA match on transplantation outcome in 1061 cord blood recipients with hematologic malignancies. Blood. 2010; 115:1843–1849. [PubMed: 20029048]
13. Shpall EJ, Quinones R, Giller R, Zeng C, Baron AE, Jones RB, et al. Transplantation of *ex vivo* expanded cord blood. Biol Blood Marrow Transplant. 2002; 8:368–376. [PubMed: 12171483]
14. Shpall EJ, Bollard CM, Brunstein C. Novel cord blood transplant therapies. Biol Blood Marrow Transplant. 2011; 17(1 Suppl):S39–S45. [PubMed: 20951821]
15. Reisner Y, Hagin D, Martelli MF. Haploidentical hematopoietic transplantation: current status and future perspectives. Blood. 2011; 118:6006–6017. [PubMed: 21921045]
16. Sorror ML, Maris MB, Storb R, Baron F, Sandmaier BM, Maloney DG, et al. Hema-topoietic cell transplantation (HCT)-specific comorbidity index: a new tool for risk assessment before allogeneic HCT. Blood. 2005; 106:2912–2919. [PubMed: 15994282]
17. Artz AS. Comorbidity and beyond: pre-transplant clinical assessment. Bone Marrow Transplant. 2005; 36:473–474. [PubMed: 16136150]

18. Artz AS, Pollyea DA, Kocherginsky M, Stock W, Rich E, Odenike O, et al. Performance status and comorbidity predict transplant-related mortality after allogeneic hematopoietic cell transplantation. Biol Blood Marrow Transplant. 2006; 12:954–964. [PubMed: 16920562]
19. Baker KS, Davies SM, Majhail NS, Hassebroek A, Klein JP, Ballen KK, et al. Race and socioeconomic status influence outcomes of unrelated donor hematopoietic cell transplantation. Biol Blood Marrow Transplant. 2009; 15:1543–1554. [PubMed: 19896078]
20. Baker KS, Loberiza FR Jr, Yu H, Cairo MS, Bolwell BJ, Bujan-Boza WA, et al. Outcome of ethnic minorities with acute or chronic leukemia treated with hematopoietic stem-cell transplantation in the United States. J Clin Oncol. 2005; 23:7032–7042. [PubMed: 16145067]
21. Serna DS, Lee SJ, Zhang MJ, Baker S, Eapen M, Horowitz MM, et al. Trends in survival rates after allogeneic hematopoietic stem-cell transplantation for acute and chronic leukemia by ethnicity in the United States and Canada. J Clin Oncol. 2003; 21:3754–3760. [PubMed: 14551294]
22. Silla L, Fischer GB, Paz A, Daudt LE, Mitto I, Katz B, et al. Patient socioeconomic status as a prognostic factor for allo-SCT. Bone Marrow Transplant. 2009; 43:571–577. [PubMed: 18978820]
23. Wheatley K, Gray R. Commentary: Mendelian randomization--an update on its use to evaluate allogeneic stem cell transplantation in leukaemia. Int J Epidemiol. 2004; 33:15–17. [PubMed: 15075139]

Table 1

Baseline patient characteristics

	Donor (n = *448*)	*No donor* (n = *83*)	P
Age at search initiation (years) (median, range)	51 (17–72)	48 (22–70)	0.43
Gender			
Male	251 (57%)	46 (56%)	0.90
Female	187 (43%)	36 (44%)	
Race			
White, non-Hispanic	354 (79%)	41 (49%)	<0.0001
Hispanic	59 (13%)	19 (23%)	
Black/African American	34 (8%)	21 (25%)	
Asian	1 (< 1%)	2 (2%)	
SES (household income) (median, range)	$40247 (20 148–100 000)	$40788 (22 395–100 481)	0.60
KPS at search initiation			
100	71 (16%)	18 (22%)	0.56
90	159 (35%)	28 (34%)	
80	89 (20%)	16 (19%)	
≤70	27 (6%)	2 (2%)	
NA	102 (23%)	19 (23%)	
Disease			0.012
AML	153 (34%)	19 (23%)	
ALL	40 (9%)	17 (20%)	
MDS/MPD	105 (23%)	15 (18%)	
MM/NHL/HD/CLL	133 (30%)	27 (33%)	
SAA/PNH	17 (4%)	5 (6%)	
CIBMTR risk category			
High	212 (47%)	32 (39%)	0.51
Intermediate	72 (16%)	16 (19%)	
Low	118 (26%)	27 (33%)	
Non-malignant	17 (4%)	4 (5%)	
Other	29 (6%)	4 (5%)	
CMV serostatus			
Positive	261 (58%)	53 (64%)	0.32
Negative	138 (31%)	19 (23%)	
NA	49 (11%)	11 (13%)	

Abbreviations: CIBMTR = Center for International Blood and Marrow Transplantation Research; HD = Hodgkin lymphoma; KPS = Karnofsky performance status; MDS = myelodysplastic syndrome; MM = multiple myeloma; MPD = myeloproliferative disorder; NHL = non-Hodgkin lymphoma; PNH = paroxysmal nocturnal hemoglobinuria; SAA = severe aplastic anemia; SES = socioeconomic status.

Table 2
Patient, disease and transplantation variables according to KPS grouping

	KPS ≥ 90	*KPS ≤ 80 or NA*	*Total*	P-*value*
Age (median, range)	51 (17–72)	50 (19–70)	531	0.31
Gender				
Female	109 (40.7%)	114 (45.2%)	223	0.330
Male	159 (59.3%)	138 (54.8%)	297	
Disease type				
ALL	20 (7.2%)	37 (14.5%)	57	0.026
AML	84 (30.4%)	88 (34.5%)	172	
MDS/MPD	65 (23.6%)	55 (21.6%)	120	
MM/NHL/HD/CLL	93 (33.7%)	67 (26.3%)	160	
SAA/PNH	14 (5.1%)	8 (3.1%)	22	
CIBMTR				
High	119 (43.1%)	125 (49.0%)	244	0.566
Intermediate	48 (17.4%)	40 (15.7%)	88	
Low	78 (28.3%)	67 (26.3%)	145	
Other or non-Malignant	31 (11.2%)	23 (9.0%)	54	
Race				
Asian	2 (0.7%)	1 (0.4%)	3	0.765
Black	28 (10.1%)	27 (10.6%)	55	
Caucasian	209 (75.7%)	186 (72.9%)	395	
Hispanic	37 (13.4%)	41 (16.1%)	78	
Donor vs no donor				
Donor	230 (83.3%)	218 (85.5%)	448	0.550
No donor	46 (16.7%)	37 (14.5%)	83	
Match				
7/8	79 (34.3%)	80 (36.7%)	159	0.622
8/8	151 (65.7%)	138 (63.3%)	289	

Abbreviations: CIBMTR = Center for International Blood and Marrow Transplantation Research; HD = Hodgkin lymphoma; KPS = Karnofsky performance status; MDS = myelodysplastic syndrome; MM = multiple myeloma; MPD = myeloproliferative disorder; NHL = non-Hodgkin lymphoma; PNH = paroxysmal nocturnal hemoglobinuria; SAA = severe aplastic anemia; SES = socioeconomic status.

Table 3

Multivariable analysis results

Variable	*Level*	*Hazard ratio*	*95% CI*	P-*value*
Age (per 10 year increase)		1.13	1.02–1.25	0.01
Disease (ref: others)	AML/ALL	1.96	1.52–2.54	< 0.0001
CIBMTR risk (ref: others)	High	2.15	1.66–2.78	< 0.0001
Donor vs no donor and KPS (ref: no donor and KPS≥90)	Donor and KPS≥90	0.59	0.38–0.90	0.016

Abbreviations: CIBMTR = Center for International Blood and Marrow Transplantation Research; KPS = Karnofsky performance status.

Table 4

Causes of death

	Donor* N = *448 (%)	***No donor* N = *83 (%)***
Relapse/progression	111 (25)	28 (34)
Not available	64 (14)	13 (16)
Infection	39 (9)	6 (7)
Transplant complications	27 (6)	1 (1)
Second malignancy	3 (1)	0 (0)
Accidental	1 (0)	0 (0)