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Rapid Donor Identification Improves Survival in High-Risk First-Remission Patients With Acute Myeloid Leukemia

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QUESTION ASKED: Could a prospective, organized effort rapidly identify alternative donors to improve the historical 40% allogeneic hematopoietic cell transplantation (HCT) rate for patients with high-risk acute myeloid leukemia (AML) in first remission to our goal of getting ≥ 60% of adults < 60 years of age with high-risk AML in first complete remission (CR1) to allogeneic HCT? In addition, does performing transplantations in significantly more adults with high-risk AML in CR1 lead to an improved outcome compared with the historical relapse-free survival of 22%?

SUMMARY ANSWER: In a newly diagnosed adult patient population with AML 18-60 years of age, early cytogenetic testing and an organized effort to identify a suitable allogeneic donor led to transplantation in 65% of high-risk patients who achieved CR1. This approach seemed to result in a significant improvement in overall survival compared with patients who did not undergo transplantation.

WHAT WE DID: We studied whether a disciplined, organized process could increase the number of patients with high-risk AML who could successfully receive an allogeneic HCT compared with historical controls.

WHAT WE FOUND: The study results suggest that better outcomes among these poor prognostic patients can be achieved by a simple approach of early HLA typing, donor identification, and expedited referral for HCT.

BIAS, CONFOUNDING FACTORS, DRAWBACKS: We used a prospective organized approach to rapidly identify donors to improve the allogeneic HCT rate in adults with high-risk AML in CR1. Despite the rigorous study design, not all confounding factors and biases could be eliminated. For example, data were not collected to determine, in the participating centers, whether having a transplantation program could influence referral patterns and rates of HCT.

REAL-LIFE IMPLICATIONS: The results of this study demonstrate the impact of early HLA typing and transplantation consultation. However, a gap still remains between large comprehensive cancer organizations and smaller community centers. As such, HCT centers will be encouraged to increase their outreach to community cancer groups that refer patients for transplantation and educate them on the importance of early HLA typing and transplantation consultation. HCT centers can share resources that are available from the National Marrow Donor Program/Be The Match to both clinicians and patients to help navigate them through and educate them about the transplantation process.

ASSOCIATED CONTENT

Appendix

Data Supplement

Author affiliations and disclosures are available with the complete article at ascopubs.org/journal/op.

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CARE DELIVERY

original contributions

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abstract

PURPOSE Patients with acute myeloid leukemia with high-risk cytogenetics in first complete remission (CR1) achieve better outcomes if they undergo allogeneic hematopoietic cell transplantation (HCT) compared with consolidation chemotherapy alone. However, only approximately 40% of such patients typically proceed to HCT.

METHODS We used a prospective organized approach to rapidly identify donors to improve the allogeneic HCT rate in adults with high-risk acute myeloid leukemia in CR1. Newly diagnosed patients had cytogenetics obtained at enrollment, and those with high-risk cytogenetics underwent expedited HLA typing and were encouraged to be referred for consultation with a transplantation team with the goal of conducting an allogeneic HCT in CR1.

RESULTS Of 738 eligible patients (median age, 49 years; range, 18-60 years of age), 159 (22%) had high-risk cytogenetics and 107 of these patients (67%) achieved CR1. Seventy (65%) of the high-risk patients underwent transplantation in CR1 ($P < .001$ compared with the historical rate of 40%). Median time to HCT from CR1 was 77 days (range, 20-356 days). In landmark analysis, overall survival (OS) among patients who underwent transplantation was significantly better compared with that of patients who did not undergo transplantation (2-year OS, 48% *v* 35%, respectively [$P = .031$]). Median relapse-free survival after transplantation in the high-risk cohort who underwent transplantation in CR1 (n = 70) was 11.5 months (range, 4-47 months), and median OS after transplantation was 14 months (range, 4-44 months).

CONCLUSION Early cytogenetic testing with an organized effort to identify a suitable allogeneic HCT donor led to a CR1 transplantation rate of 65% in the high-risk group, which, in turn, led to an improvement in OS when compared with the OS of patients who did not undergo transplantation.

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INTRODUCTION

The prognosis of adults with acute myeloid leukemia (AML) can be estimated using a variety of methods, but cytogenetics has remained the most common and reproducible. Using cytogenetics, patients can be categorized as having favorable-, intermediate-, or unfavorable (high)-risk disease per updated SWOG criteria analogous to 2017 European Leukemia Network risk stratification.[1-7] In a previous intergroup trial for adult patients with AML who were ≤ 60 years of age, 30% of patients had unfavorable risk, had a first complete remission (CR1) rate of 54%, and had a 5-year survival of 11%, outcomes that were significantly worse than those seen in intermediate- or favorable-risk patients.[8-10] In this prior trial, patients with matched siblings were assigned to receive an allogeneic hematopoietic cell transplant (HCT) in CR1, whereas those without a matched sibling were randomly assigned to autologous transplantation or additional chemotherapy. However, only 40% of patients assigned to allogeneic HCT actually underwent transplantation. Although the rates of HCT have likely increased for high-risk patients over the past years, the process of early patient identification and HLA typing remains important to the oncology community at large.

On the basis of an intent-to-treat analysis, 5-year survival after CR1 was 52% for allogeneic transplantation, 42% for autologous transplantation, and 39% for chemotherapy. The advantage of allogeneic transplantation was most obvious for patients with high-risk disease, with a 5-year survival of 44% with allogeneic transplantation versus 15% with chemotherapy alone.[8] On the basis of results from this and similar trials, allogeneic transplantation from a matched related donor has

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been recommended for adults ≤ 60 years of age with high-risk AML in CR1.[7,11-13]

Unfortunately, < 30% of adults will have HLA-matched relatives able to donate hematopoietic stem cells.[14-16] Alternative donors are available for the majority of patients with high-risk AML, and outcomes of transplantation should approximate those seen with matched related donors.[17,18] Recent data suggest that outcomes after allogeneic HCT from fully matched unrelated donors, as with using cord blood or haplo-identical related donors as a stem cell source, seem to be similar to that after matched related donor transplantation.[17,19-22] However, it takes time, effort, and resources to identify potential donors, and there are no prospective data addressing how often this can actually be accomplished. In addition, there are no published prospective studies of the outcome of alternative donor transplantations for a large cohort of adult patients with high-risk AML identified at diagnosis that would allow for an estimation of the impact of HCT on survival. Thus, we studied whether a disciplined, organized process could increase the number of patients with high-risk AML who could successfully receive an allogeneic HCT compared with historical controls.

METHODS

Study Design

SWOG-led intergroup study S1203 (ClinicalTrials.gov identifier: NCT01802333) was an open-label, multicenter, phase III trial in patients with previously untreated AML who were 18-60 years of age. It had 2 primary objectives: a random assignment among 3 induction therapies and a transplantation objective for high-risk patients who achieve CR1 on protocol. Patient accrual occurred between December 15, 2012, and November 4, 2015. The induction phase randomly assigned patients to receive standard cytarabine plus daunorubicin (7+3) therapy or idarubicin with high-dose cytarabine (IA) or IA with vorinostat (IA+V). The 7+3 and IA arms each enrolled 261 eligible patients, and the IA+V arm enrolled 216 (Fig 1A). The IA+V arm of the study was closed early because of futility. The results of the induction question will be reported separately (G. Garcia-Manero, personal communication, December 2019). The data cutoff for this report was January 29, 2018. The study protocol was conducted according to the Declaration of Helsinki and with approval of the protocol from local institutional review boards. All participants provided written informed consent before participating in this study. The study was designed by 6 of the authors, and the data were collected and analyzed by all the authors, who vouch for the accuracy and completeness of the data and analyses and for the adherence of the study to the protocol. No one who is not an author contributed to the writing of the manuscript.

At the time of induction random assignment (study entry), all patients had a buccal swab sent directly to the National Marrow Donor Program to facilitate HLA typing (Fig 1B). At the same time, all patients had conventional cytogenetic analysis performed locally for risk stratification, with an expected turnaround time of 7-10 days. Study staff followed up with sites that had not submitted results within 10 days and did so every 7-10 days thereafter to ensure timely determination of risk. Using updated SWOG criteria, high-risk classification was defined as del(5q)/−5, del(7q)/−7, abn3q26 [inv(3)/t(3;3)], 11q23 rearrangement [except t(9;11)], del(17p), t(6;9) t(9;22) complex (at least 3 unrelated abnormalities), and monosomal karyotype (either loss of 2 different chromosomes or loss of 1 chromosome together with a structural chromosome abnormality other than add, ring, and mar).[1,5,6] All patients found to have high-risk cytogenetics had expedited HLA typing, and a preliminary search for an alternative donor was performed. The search results and donor selection recommendations were sent to the referring physician within 5 days of completion of HLA typing. This approach contrasts with the typical donor search process, which relies on HLA typing and initiation of a formal search by the patient's transplantation center after referral and consultation. The high-risk patients were expected to be referred to a transplantation center for consultation with the goal of conducting an allogeneic transplantation at any point in the patient's CR1 (including those with incomplete count recovery). The schema for donor identification is shown in Figure 1C. Decisions regarding donor selection and transplantation were at the discretion of the treating physician, the transplantation center, and the patient. As appropriate, siblings were also typed and, if matched, could then serve as a donor. In addition, unrelated donors or umbilical cord blood units were identified, qualified, and procured as appropriate. Supportive care was provided as per institutional practice.

Patients

Patients ≥ 18 and ≤ 60 years of age with morphologically confirmed, newly diagnosed AML using standard WHO diagnostic criteria were eligible for the study. Additional details regarding the study design and eligibility are provided in the Data Supplement (online only).

Safety and Efficacy Definitions

Adverse events were graded according to the National Cancer Institute Common Terminology Criteria for Adverse Events, Version 4.0. Efficacy end points included complete remission (CR), complete remission with incomplete blood count recovery (CRi), relapse-free survival (RFS), and overall survival (OS). Morphologic CR was defined by international working group criteria including documentation of an absolute neutrophil count ≥ 1,000/μL, platelet count ≥ 100,000/μL, < 5% bone marrow blasts, no Auer rods, and no evidence of extramedullary disease.[23] For morphologic CRi, absolute neutrophil count could be < 1,000/μL and/or platelet count < 100,000/μL. RFS was measured from the date of CR/CRi until relapse or death from

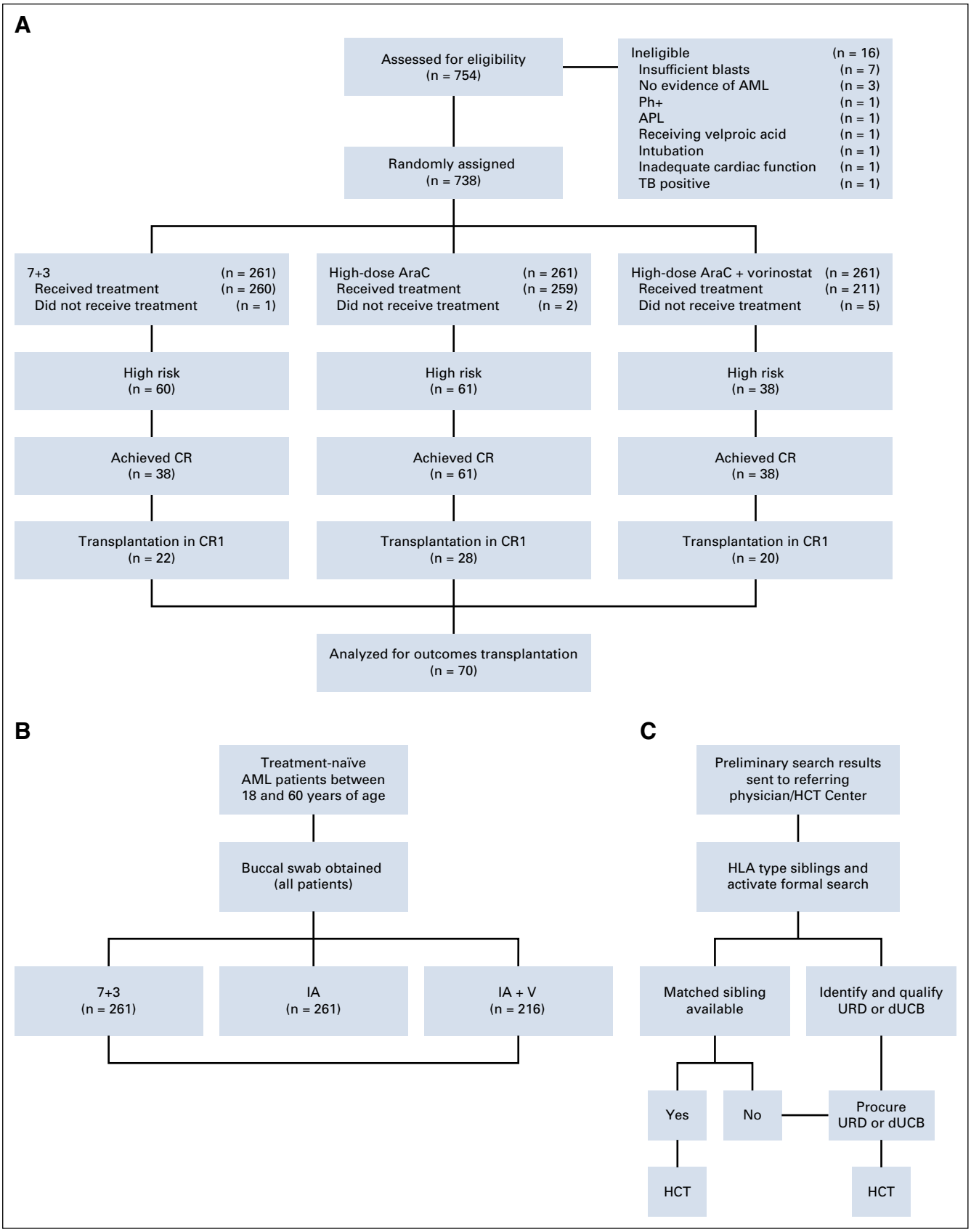

FIG 1. (A) Consort diagram displaying random assignment and distribution of patients. Diagram shows patient flow through the initial induction stage of the S1203 controlled trial (eligibility and random assignment) with depiction of those high-risk patients in each arm who (continued on following page)

any cause, and patients last known to be alive without relapse were censored at date of last contact. OS was measured from the date of random assignment to death from any cause, and patients last known to be alive were censored at the date of last contact.

Statistical Design and Methods

The transplantation objective was powered to evaluate whether it was possible to conduct allogeneic HCT on ≥ 60% of adults with high-risk AML in CR1 (alternative hypothesis). If ≤ 40% of high-risk patients in CR underwent transplantation, the proposed transplantation support system would not be considered successful (null hypothesis, which was based on the historical rate from SWOG trial S9034).[8] We estimated that 53 patients would provide 89% power for this test with a one-sided α level of 4%. RFS and OS were estimated using the Kaplan-Meier method and were compared between groups using log-rank tests. The cumulative incidence of transplantation was calculated considering death and/or relapse as competing events. Cox regression models were used to evaluate covariate associations with RFS and OS. Landmark and time-dependent covariate analyses were used to control for survival by response bias when comparing patients who underwent transplantation and those who did not.[24] *P* values are 2 sided unless stated otherwise.

RESULTS

Patient Flow and Characteristics

Overall, 738 patients were enrolled in this study, with a median age of 49 years (range, 18-60 years; cohort characteristics in Table 1). Cytogenetic risk at enrollment included 159 patients (22%) with high risk, 457 (63%) with intermediate risk, and 96 (13%) with favorable risk; 26 patients (4%) had missing/unknown cytogenetic risk. Sixty patients (23%) in the 7+3 arm, 61 (23%) in the IA arm, and 38 (17%) in the IA+V arm had high-risk cytogenetics. Among all 738 patients, 370 (50%) received an allogeneic HCT in CR1. Of the 159 patients with high-risk cytogenetics, 107 (67%) achieved a CR/CRi at a median of 33 days (range, 12-88 days) after random assignment. Of these 107 high-risk patients in CR1, 70 (65%) went on to receive a transplant in CR1. This transplantation rate was significantly higher than the historical rate of 40% (1-sided and 2-sided $P < .001$).

Transplantation recommendations for the intermediate-risk group were not outlined in the trial protocol. The rate of HCT in the intermediate-risk group was 40%, close to the historical high-risk rate. Although a comparison between the rate of HCT in the intermediate-risk and high-risk groups is problematic for many reasons, including various practice patterns across institutions because not all sites have intermediate-risk patients undergo transplantation equally aggressively, as well as other biases that cannot be measured easily, the *P* value for the comparison with the high-risk group was < .001.

Among the 70 high-risk CR1 patients who underwent transplantation, 25 (36%) received their transplant from matched-related donors, 32 (46%) from matched-unrelated donors, 4 (4%) from mismatched-related donors, and 8 (11%) from mismatched-unrelated donors, and 1 (1%) received an umbilical cord blood transplant (Appendix Table A1, online only).

Thirty-seven high-risk CR1 patients did not receive a transplant. Reasons included the following: 6 patients relapsed; 6 patients died before HCT; 3 patients because of comorbidities, insurance issues, or lack of an appropriate donor; 3 patients because of physician decision; 2 patients elected against HCT; 9 patients for other reasons; and 8 patients did not report a reason (Appendix Table A2, online only). The cumulative incidence of HCT among the 107 high-risk patients who had achieved CR1 was 40% by 3 months after CR1, 56% by 4 months, 63% by 6 months, and 66% by 12 months (Fig 2A). Among patients who underwent transplantation in CR1, the median time to HCT from CR1 was 2.5 months (range, 0.6-12 months). The cumulative incidence of HCT among all high-risk patients (n = 159) is shown in Figure 2B. There was a nonsignificant trend of higher rates of transplantation in university-based institutions: 70% of the patients from university-based institutions underwent transplantation versus 48% from non–university-based community institutions ($P = .074$).

Efficacy

Median follow-up of living patients was 31 months. Median RFS in the high-risk CR1 cohort, including patients who did not undergo transplantation, was 10 months; median RFS after HCT was 11.5 months. Median OS among the 159 high-risk patients was 12 months. Among the 70 patients who underwent transplantation in CR1, the median OS after transplantation was 14 months. The 2-year OS in the entire cohort was 31%, and the 2-year OS after HCT for those who underwent transplantation in CR1 was 42%. In a landmark analysis of patients alive 6 months after random assignment (to control for survival by response bias),[24] high-risk patients who had received a transplant in

FIG 1. (Continued). achieved complete remission (CR) and subsequently underwent transplantation in first CR (CR1). Flow charts outlining (B) the method for patient assessment of high-risk cytogenetics at study entry and (C) the expedited donor identification and transplantation procedure for patients with high-risk acute myeloid leukemia (AML). Panel B shows the process of obtaining a buccal swab at time of diagnosis and study entry before random assignment to induction therapy, with expedited human leukocyte antigen (HLA) typing performed within 5 business days for patients with high-risk cytogenetics. Panel C depicts flow for determining appropriate donor identification for hematopoietic cell transplantation (HCT) of high-risk patients in CR1. 7+3, standard cytarabine plus daunorubicin; APL, acute promyelocytic leukemia; AraC, cytarabine; dUCB, double umbilical cord blood; IA, idarubicin with high-dose cytarabine; IA+V, IA with vorinostat; Ph+, Philadelphia chromosome positive; TB, tuberculosis; URD, unrelated donor.

TABLE 1. Summary of High-Risk Patients Who Achieved CR, by Transplantation Status

Factor	CR1 (n = 107)	High-Risk CR1 Transplantation (n = 70)	High-Risk CR1 Nontransplantation (n = 37)	*P*
7+3	38 (36)	22 (31)	16 (43)	.53
IA	40 (37)	28 (40)	12 (32)	
IA+V	29 (27)	20 (29)	9 (24)	
Age, years	50 (18,60)	48 (19, 60)	54 (18, 60)	.03
White	91 (85)	60 (86)	31 (84)	.69
Black	7 (7)	4 (6)	3 (8)	
Asian	2 (2)	1 (1)	1 (3)	
> 1 ethnicity	1 (1)	0 (0)	1 (3)	
Unknown ethnicity	4 (4)	3 (4)	1 (3)	
Native American	2 (2)	2 (3)	0 (0)	
Hispanic	9 (8)	2 (3)	7 (19)	.0077
Not Hispanic	98 (92)	68 (97)	30 (81)	
Female	46 (43)	28 (40)	18 (49)	.42
Male	61 (57)	42 (60)	19 (51)	
PS 0-1	97 (91)	65 (93)	32 (86)	.31
PS 2-3	10 (9)	5 (7)	5 (14)	
WBC, 10^3	4.1 (0.4, 160)	4 (0, 138)	4 (1, 160)	.95
Platelets, 10^3	47 (6, 1,800)	48 (6, 1,800)	34 (7, 348)	.24
Marrow blasts, %	51 (0, 94)	50 (5, 94)	53 (0, 93)	.96
Blood blasts, %	17 (0, 99)	11 (0, 99)	21 (0, 79)	.26
Hemoglobin, g/dL	8.6 (3.8, 72)	9 (4, 15)	9 (6, 72)	.8
ITD	6 (6)	3 (4)	3 (8)	.5
Point mutation	3 (3)	3 (4)	0.(0)	
FLT3−	59 (55)	37 (53)	22 (59)	
Unknown	39 (36)	27 (39)	12 (32)	
NPM1+	3 (3)	3 (4)	0 (0)	.45
NPM1−	60 (56)	37 (53)	23 (62)	
Unknown	44 (41)	30 (43)	14 (38)	
CEBPA−	35 (33)	21 (30)	14 (38)	.49
Unknown	70 (65)	48 (69)	22 (59)	
Single mutation	2 (2)	1 (1)	1 (3)	

NOTE. Data are presented as median (range) or No (%).

Abbreviations: 7+3, standard cytarabine plus daunorubicin; CEBPA, CCAT enhancer binding protein alpha; CR, complete remission; CR1, first CR; FLT, fms tyrosine kinase; IA, idarubicin with high-dose cytarabine; IA+V, IA with vorinostat; ITD, internal tandem duplication; NPM1; nucleophosinin 1; PS, performance status.

CR1 had significantly better OS (hazard ratio [HR], 0.60; 95% CI, 0.38 to 0.95; $P = .031$; 2-year OS among those who underwent transplantation in CR1 was 48% *v* 35% for everyone else; Fig 3A) compared with high-risk patients who had not received a transplant in CR1; in the subset of patients alive without relapse at 6 months, RFS was not significantly different between those who had received a transplant in CR and everyone else (HR, 0.82; 95% CI, 0.42 to 1.60; $P = .56$; Fig 3B). Time-dependent covariate models had results similar to those of the landmark analyses.

Among all high-risk patients, in multivariable analyses (controlling for induction treatment arm, age, sex, performance status, baseline WBC, platelets, bone marrow blasts, peripheral blood blasts, hemoglobin, and HCT in CR1), the type of institution (university *v* community) was not significantly associated with OS (HR, 0.89; 95% CI, 0.55 to 1.44; $P = .63$) or RFS (HR, 1.05; 95% CI, 0.56 to 1.97; $P = .87$). There was no evidence of an association between time to transplantation after CR1 and outcome after transplantation (RFS after transplantation HR, 0.999; 95% CI,

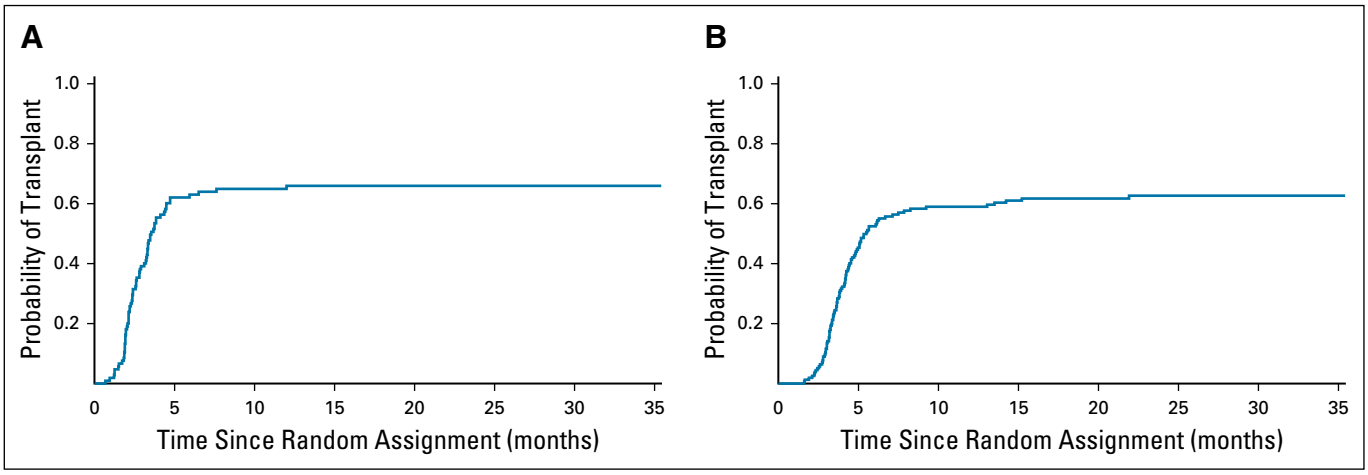

FIG 2. Cumulative incidence of transplantation among high-risk patients in first complete remission (CR1) and all high-risk patients. (A) Cumulative incidence of receiving a transplant (with relapse and death as competing events) among the 107 high-risk patients who had achieved CR1 was 13% by 3 months after CR1, 38% by 4 months, 54% by 5 months, 60% by 6 months, and 65% by 9 months. (B) Cumulative incidence of transplantation among all high-risk patients (n =159, death as the competing event) was 11% by 3 months after registration, 33% by month 4, 46% by month 5, 53% by month 6, 58% by month 9, and 60% by month 13.

0.99 to 1.01; $P = .92$; OS after transplantation HR, 1.002; 95% CI, 0.99 to 1.01; $P = .48$).

RFS and OS after HCT were not significantly different among high-risk patients who were treated using a matched related donor versus a matched unrelated transplant (related donor = reference: RFS HR, 0.69; 95% CI, 0.36 to 1.31; $P = .26$ [Fig 3C] and OS HR, 0.77; 95% CI, 0.39 to 1.52; $P = .46$ [Fig 3D]; Appendix Table A3, online only), although the sample size for this comparison was modest and the CIs wide. Fifty-eight patients received a myeloablative conditioning regimen, and 13 patients received a reduced-intensity conditioning regimen (intensity not reported for 3 patients); recognizing the small patient numbers, there was no significant difference in OS after transplantation on the basis of conditioning regimen (reference was myeloablative: HR, 1.55; 95% CI, 0.64 to 3.71; $P = .32$), and RFS was nonsignificantly worse among patients who received reduced-intensity conditioning (HR, 2.13; 95% CI, 0.96 to 4.80; $P = .068$).

DISCUSSION

The data from this prospective study, which attempted to expeditiously find allogeneic stem cell donors, support 2 major conclusions. First, for patients with AML who are in first CR and who have high-risk cytogenetics, it is possible to get ≥ 60% of adults ≤ 60 years of age to HCT. Second, by getting more high-risk patients to transplantation, there seemed to be, relative to patients who did not undergo transplantation, an improvement in OS for the overall high-risk patient population. This was not a prospective randomized comparison, and other factors, including not knowing whether having a transplantation program among the participating centers may have influenced referral patterns, rates of HCT, and/or the improved outcomes, may have affected the results.

Depending on ethnicity, matched unrelated adult donors can be found for anywhere from 25% to 70% of patients without a matched related donor.[16,18,22,25,26] In addition, registry data and data from single institutions and cooperative groups show that transplantation outcomes after myeloablative preparative regimens are similar using matched sibling, matched unrelated, or cord blood transplants.[16-22,25-28] Data also suggest that transplantations using haplo-identical donors can provide similar outcomes.[29-34] Theoretically, lack of a matched sibling donor (available in approximately 33%) should not be a barrier to HCT because alternative donors are available for the majority of patients with high-risk AML. Interestingly, the HCT rate seemed to be different in Hispanic versus non-Hispanic patients. Because this was not a prespecified comparison with small numbers of Hispanic patients—without independent (external) data finding the same pattern—we are unable to know if this is just a spurious association in our data set or indicative of a larger pattern in transplantation of Hispanic patients.

Single-institution studies and large meta-analyses have led to the recommendation by most experts, including the recently published European LeukemiaNet, that patients with unfavorable risk AML, now defined by a combination of cytogenetics and mutational analysis, be treated with allogeneic HCT if possible.[9,35-38] Although we solely used conventional cytogenetics to characterize risk in this study, additional routine mutational testing should be used for detecting high-risk features associated with poor prognosis after chemotherapy consolidation to identify those who will potentially benefit from expedited referral for transplantation.

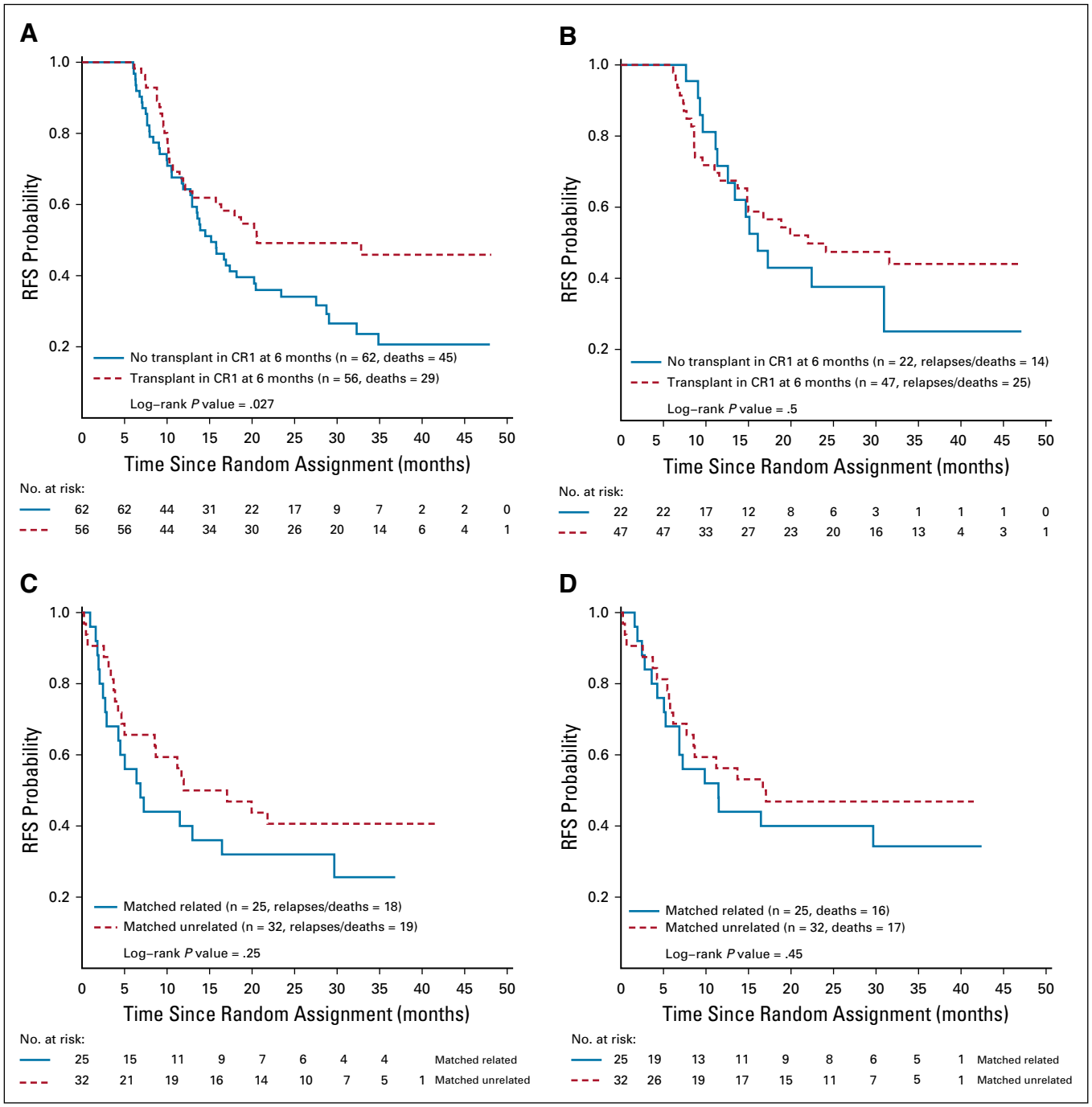

FIG 3. Survival outcomes for patients transplanted in CR1. (A) Landmark analysis for OS and (B) RFS among patients alive after 6 months after randomization. (C) RFS and (D) OS among CR1 high-risk patients who were treated using a matched related donor *v* a matched unrelated donor. CR1, first complete remission; OS, overall survival; RFS, relapse-free survival.

Our results make intuitive sense because the process to find and coordinate suitable donors can be long and difficult. Therefore, beginning the process as early as possible should improve the chances of finding suitable donors and allow more time to address other barriers to transplantation (including insurance or patient support). At many comprehensive cancer centers, standard practice for all patients with AML includes HLA typing at the time of diagnosis and early consultation with transplantation physicians. However, outside of such centers, patients are often HLA typed and are referred late to transplantation facilities. Reasons for not HLA typing at diagnosis include a lack of access to HLA-typing services, a lack of insurance coverage, and a lack of awareness of the benefit of early HLA typing and transplantation consultation.

The results of this study demonstrate the impact of early HLA typing and transplantation consultation. However, a gap still remains between large comprehensive cancer organizations and smaller community centers. As such, HCT centers will be encouraged to increase their outreach to community cancer groups that refer patients for transplantation and educate them on the importance of early HLA typing and transplantation consultation. HCT centers can share resources that are available from the National Marrow Donor Program/Be The Match to both clinicians and patients to help navigate them through and educate them about the transplantation process.

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PRIOR PRESENTATION

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AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

Rapid Donor Identification Improves Survival in High-Risk First-Remission Patients With Acute Myeloid Leukemia

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APPENDIX

TABLE A1. HCT Donor Sources for S1203 Patients Who Underwent Transplantation (n = 70)

HCT Donor Source	No. (%)
MRD	25 (36)
MUD	32 (46)
Mismatched related donor	4 (4)
Mismatched unrelated donor	8 (12)
UCB	1 (1)

Abbreviations: HCT, hematopoietic cell transplantation; MRD, matched related donor; MUD, matched unrelated donor; UCB, umbilical cord blood.

TABLE A2. Reasons CR1 Patients Did Not Receive HCT (n = 37)

Reason	No.
Relapse	6
Comorbidities	1
Death	6
Physician decision	3
Patient decision	2
No insurance	1
No donor identified	1
Other	9
Unknown	8

Abbreviations: CR1, first complete remission; HCT, hematopoietic cell transplantation.

TABLE A3. One-Year Estimates of Survival for High-Risk Patients Who Underwent Transplantation in CR1

Donor	RFS (95% CI)	OS (95% CI)
MRD	40 (25 to 65)	44 (28 to 69)
MUD	50 (35 to 71)	56 (41 to 76)

NOTE. The hazard ratio (reference = related) for relapse-free survival (RFS) after transplantation was 0.69 (95% CI, 0.36 to 1.32) and for overall survival (OS) after transplantation was 0.77 (95% CI, 0.39 to 1.52).

Abbreviations: CR1, first complete remission; MRD, matched related donor; MUD, matched unrelated donor.