MDS disease characteristics, not donor source, predict hematopoietic stem cell transplant outcomes

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INTRODUCTION

Myelodysplastic syndromes (MDS) are a complex and heterogeneous group of clonal hematopoietic stem cell disorders for which the only known cure is allogeneic stem cell transplantation (HCT). Few studies comparing MDS HCT outcomes between sibling and umbilical cord blood (UCB) donors exist. Using the University of Minnesota Blood and Marrow Transplant (BMT) database, we retrospectively analyzed HCT outcomes among 89 MDS patients undergoing either sibling or double UCB HCT in 2000–2013. We observed similar survival, relapse and non-relapse mortality between sibling and UCB donor sources. Relapse was increased in those with monosomy 7 karyotype (P = 0.04) and with reduced intensity conditioning (P < 0.01). In summary, our data highlight similar MDS HCT outcomes regardless of donor source and support the use of UCB as an alternative donor when a sibling is unavailable.

METHODS

Data source

Through the University of Minnesota Blood Marrow Transplant (BMT) database, we identified 89 consecutive adult patients (>18 years of age) with MDS who underwent MA or RIC allogeneic HCT using either sibling or double UCB donors from 2000 to 2013.

Data collection

All patients were treated on protocols reviewed and approved by the University of Minnesota Institutional Review Board and all participating subjects provided informed consent according to the principles of the Declaration of Helsinki before proceeding to transplant. Data were prospectively collected in the institutional BMT database.

End points and definitions

The primary end point was an outcome comparison between recipients of sibling or UCB donor sources in a more homogenous patient population with consistent conditioning platforms, we retrospectively analyzed HCT outcomes among MDS patients undergoing either sibling or double UCB allogeneic stem cell transplant at our institution.
Diagnostic specimens were reviewed by institutional hematopathologists and classified by the 2008 World Health Organization (WHO) MDS criteria.13 Therapy-related MDS was defined clinically as MDS following exposure to alkylating agents, topoisomerase II inhibitors or radiotherapy. Blast percentage categories (≤2%, >2–<5, 5–10 and >10) were chosen to distinguish patients with deeper levels of remission (≤2% versus MK) on 5-year OS and DFS.23 Fine and Gray proportional hazards regression was used to assess the independent effect of donor type and cytogenetic classification (R-IPSS cytogenetic classification versus MK) on NRM, relapse, engraftment and GVHD.24 Donor type and one MDS cytogenetic classification was used in each model. Other variables that remained statistically significant or confounded the effect of donor type and MDS disease characteristics were included in the models as appropriate. Visual plots and Martingale residuals were used to test against non-proportionality.25 All reported P-values were two-sided. SAS 9.3 (SAS Institute, Cary, NC, USA) and R 3.0.2 (R foundation for Statistical Computing, Vienna, Australia) were used for all statistical analyses.

RESULTS

Patient demographics

Patient disease and transplant characteristics for the 89 patients (median age 55, range 19–72 years) are included in Table 1. Patient age, gender, year of transplant, WHO categorization, disease status at transplant, Karnofsky performance score, HCT-CI, R-IPSS cytogenetics at diagnosis, presence of MK and bone marrow blasts at transplant were similar between sibling and UCB donor sources. A higher percentage of sibling donors underwent MA conditioning (47% versus 11% UCB) and accordingly more frequently used cyclosporine/methotrexate-based GVHD prophylaxis. Median follow-up of survivors was longer for siblings at 7.7 years (range 3–12.1) as compared with 3.3 years (range 3–6.2) for UCB recipients.

OS and DFS

Five-year survival for the entire group was 37%. There was no difference in survival outcomes between donor sources: 5-year survival for sibling donor and UCD recipients were 41% (95% confidence interval (CI) 26–56%) and 33% (95% CI 19–48%) (P = 0.29), respectively. (Figure 1) Conditioning did not confer a survival difference at 5 years: 39% (95% CI, 20–58%) for MA compared with 40% (95% CI, 25–55%) for RIC with ATG and 30% (95% CI, 11–51%) for RIC without ATG (P = 0.80) (Table 2).

HCT outcomes in MDS

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Table 1. Patient demographics

| Variable                  | Siblings (n=45) | UCB (n=44) | P-value |
|---------------------------|-----------------|------------|---------|
| N                         | 45              | 44         |         |
| Age (years); median (IQR) | 55 (27–71)      | 58 (19–72) | 0.48    |
| Age, years                |                 |            |         |
| 18–29                     | 2 (4%)          | 1 (2%)     | 0.75    |
| 30–49                     | 11 (24%)        | 9 (21%)    |         |
| 50+                       | 32 (71%)        | 34 (77%)   |         |
| Year of HCT               |                 |            |         |
| 2000–2006                 | 19 (42%)        | 13 (30%)   | 0.21    |
| 2007–2013                 | 26 (58%)        | 31 (71%)   |         |
| Patient gender: male      | 32 (71%)        | 28 (64%)   | 0.45    |
| Conditioning              |                 |            | <0.01   |
| MA                        | 21 (47%)        | 5 (11%)    |         |
| RIC: with ATG             | 17 (38%)        | 27 (61%)   |         |
| RIC: without ATG          | 7 (16%)         | 12 (27%)   |         |
| GVHD prophylaxis          |                 |            | <0.01   |
| CSA/MMF                   | 23 (51%)        | 37 (84%)   |         |
| CSA/MTX                   | 17 (38%)        | 1 (2%)     |         |
| Other                     | 5 (11%)         | 6 (14%)    |         |
| Diagnosis: WHO            |                 |            | 0.28    |
| RA/RARS/MDS unknown       | 14 (31%)        | 9 (20%)    |         |
| RAEB 1 and 2              | 19 (42%)        | 26 (59%)   |         |
| RIC/RCMD-RS               | 12 (26%)        | 9 (11%)    |         |
| Disease status            |                 |            | 0.37    |
| Untreated MDS             | 19 (42%)        | 11 (23%)   |         |
| CR                        | 2 (4%)          | 3 (7%)     |         |
| Treated—responsive        | 14 (31%)        | 19 (43%)   |         |
| Treated—resistant         | 10 (22%)        | 11 (23%)   |         |
| Prior therapy             |                 |            | 0.15    |
| No treatment              | 19 (42%)        | 11 (23%)   |         |
| Induction                 | 10 (22%)        | 19 (43%)   |         |
| HMA                       | 11 (24%)        | 12 (27%)   |         |
| Lenalidomide              | 5 (11%)         | 2 (5%)     |         |
| Therapy-related MDS, yes  | 11 (24%)        | 11 (23%)   | 0.99    |
| Karnofsky: < 90           | 9 (20%)         | 5 (11%)    | 0.26    |
| HCT-CI                    |                 |            | 0.47    |
| Low risk                  | 17 (38%)        | 13 (30%)   |         |
| Intermediate              | 16 (36%)        | 14 (32%)   |         |
| High risk                 | 12 (27%)        | 17 (39%)   |         |
| R-IPSS cytogenetic classification at DX |                 |            | 0.71    |
| Very good                 | 1 (2%)          | 1 (2%)     |         |
| Good                      | 14 (31%)        | 15 (34%)   |         |
| Intermediate              | 6 (13%)         | 7 (16%)    |         |
| Poor                      | 10 (22%)        | 13 (30%)   |         |
| Very poor                 | 14 (31%)        | 8 (18%)    |         |
| MK at Dx, present         | 17 (38%)        | 11 (23%)   | 0.19    |
| BM blasts at HCT          |                 |            | 0.11    |
| ≤2%                       | 29 (64%)        | 27 (61%)   |         |
| 3–4%                      | 7 (16%)         | 13 (30%)   |         |
| 5–10%                     | 5 (11%)         | 4 (9%)     |         |
| >10%                      | 4 (9%)          | 0          |         |
| Patient CMV: positive     | 22 (49%)        | 27 (61%)   | 0.24    |
| Follow-up, median (IQR)   | 7.7 years       | 3.3 years  | (3.0–12.1) | (3.0–6.2) |

Abbreviations: BM = bone marrow; Bu = busulfan; CSA = cyclosporine; Cy = cyclophosphamide; Dx = diagnosis; Flu = fludarabine; HCT = hematopoietic cell transplantation; HCT-CI = hematopoietic cell transplant comorbidity index; HMA = hypomethylating agents; IQR = interquartile range; MA = myeloablative; MDS = myelodysplastic syndrome; MFS = monosomal karyotype; MMF = mycophenolate mofetil; MTX = methotrexate; RA = refractory anemia; RAEB = refractory anemia with excess blasts; RARS = refractory anemia with ring sideroblasts; RCMD = refractory cytopenia with multilineage dysplasia; RIC = reduced intensity conditioning; R-IPSS = Revised International Prognostic Scoring System; UCB = umbilical cord blood; WHO = World Health Organization. Note: ‘GVHD prophylaxis—Other’; Sibling: sirolimus/tacrolimus, MTX/ATG/tacrolimus, and CSA/CD34 selection; UCB: sirolimus/MMF.

Figure 1. OS by donor type.

and 28% (95% CI, 18–38%) respectively. There was no difference in incidence of relapse at 2 years between donor sources: siblings 27% (95% CI, 13–40%) versus UCB 30% (95% CI, 16–44%), There were lower rates of 2-year relapse with MA conditioning at 12% (95% CI, 0–24%) versus RIC+ATG at 32% (95% CI, 18–46%) versus RIC with no ATG at 42% (95% CI, 19–65%), but this did not reach statistical significance (P = 0.07). (Figure 2)

Patients with MK had a higher 2-year incidence of relapse at 39% (95% CI, 21–58%) compared with 24% (95% CI, 13–35%) in those without (P = 0.03) (Figure 3). R-IPSS cytogenetic category at diagnosis was less consistent at predicting relapse in our cohort of patients as evident by rates of relapse within R-IPSS cytogenetic subgroups contrary to well-published trends. Disease status at transplant, WHO category, prior treatment, bone marrow blast percentage at transplant or therapy-related MDS did not predict relapse.

In multivariate analysis, we found no difference in risk of relapse with respect to donor source or disease status at transplant. When comparing the different MDS cytogenetic classifications, MK (RR 2.7 (95% CI, 1.0–6.9) P = 0.04) most strongly predicted relapse. Regardless of the cytogenetic model used, conditioning intensity consistently and significantly predicted RR with higher risk in the RIC groups.

NRM at day +100 was 18% for the entire cohort and was similar with respect to donor source: 16% (95% CI, 5–26%) for siblings compared with 20% (95% CI, 9–32%) for UCB. Recipients aged ≤29 years had superior survival with 0% NRM at day +100. Gender, Karnofsky performance score, HCT-CI nor year of transplant impacted NRM. Those with a bone marrow blast percentage >10% had very high NRM of 75% at day +100 (95% CI, 34–100%; P < 0.01).

One-year NRM remained relatively low for the entire cohort at 25%. In multivariate analysis, there was no difference in NRM by donor type. Conditioning did impact NRM with lower NMR with RIC compared with MA conditioning.

GVHD

Incidence of aGVHD grades II–IV at day +100 were modest at 38% (95% CI, 28–49%) for the entire cohort and were similar between donor sources. Severe aGVHD grades III–IV at day +100 were 19% overall with an incidence of 27% (95% CI, 14–40%) in siblings and 11% (95% CI, 2–21%) in UCB (P = 0.09). There was a higher incidence of severe aGVHD in those with MK at 32% (95% CI, 15–49%) compared with 14% (95% CI, 5–22%) in those without and also a higher incidence in those with >10% blasts at 50% (95% CI, 11–89%). In multiple regression analysis, there was no difference in severe aGVHD grades III–IV by donor source.

The overall incidence of cGVHD at 1 year was 31% (95% CI, 21–42%) for the entire cohort. We did observe a difference in rates of cGVHD based on donor source with a low incidence of 18% (95% CI,
DISCUSSION

Outcomes with stem cell transplant for MDS remain variable with the universal goal of identifying the most important predictors of transplant success to yield better patient and donor selection, better pre-HCT therapy selection to improve pre-HCT disease burden and identification of alternative approaches for those with only minimal chance of benefit from transplant. Our data highlighted similar outcomes regardless of sibling or UCB donor source and confirm the ability of well-established cytogenetic classification models to predict post-HCT survival and relapse in our patient population.

Abbreviations: BM = bone marrow; CI = confidence interval; DFS = disease-free survival; Dx = diagnosis; HCT = hematopoietic cell transplantation; HCT-CI = hematopoietic cell transplant comorbidity index; MA = myeloblastic; MDS = myelodysplastic syndrome; MDS-U = myelodysplastic syndrome unspecified; MK = monosomal karyotype; NRM = non-relapse mortality; OS = overall survival; RA = refractory anemia; RAEB = refractory anemia with excess blasts; RA/RARS/MDS-U = refractory anemia with ring sideroblasts; RCMD/RCMD-RS = refractory anemia with multilineage dysplasia—ring sideroblasts; R-IPSS = Revised International Prognostic Scoring System; UCB = umbilical cord blood; WHO = World Health Organization. Bold entries indicate statistically significant results.

7–30%) in the UCB cohort compared with 44% (95% CI, 28–61%) in the sibling cohort (P = 0.02). This finding was confirmed in multivariate analysis (UCB RR 0.3 (95% CI, 0.1–0.7; P < 0.01).
Sibling donors remain the donor of choice for patients requiring transplant; however, when siblings are not available controversy exists regarding the next best option. Although comparisons of sibling and unrelated donor transplants in MDS are readily available, the literature investigating UCB is less developed. Our institutional alternative donor HCT research interest has pioneered the field of UCB transplantation. When an urgent HCT is needed and few unrelated donor options are available, our institutional alternative donor choice is an UCB source. Our current data highlight similar outcomes regardless of donor source and are consistent with previous publications from our institution with respect the MDS and AML outcomes.24 To date, the largest MDS UCB outcomes analysis was a recent 2015 Eurocord-EBMT analysis highlighting the outcomes of MDS adults undergoing either UCB (n = 129) or peripheral blood MUD (n = 502) RIC HCT. In this analysis, 2-year survival ranged from 30% for UCB to 50% for MUD (P < 0.0001) with similar relapse incidence across donors (23% MUD to 30% UCB) but increased NRM at 42% for UCB compared with 31% for PB MUD (P = 0.03). Based on these data, the authors concluded that PB MUD donors were the preferred stem cell source compared with UCB in the absence of a sibling donor.27 Although the outcomes of this study highlight a much larger ‘MDS’ patient cohort, it is important to note that 65% of the MDS patients within the entire cohort had progressed to AML prior to transplantation, and of those patients, only 52% had achieved remission prior to transplant. Specifically, within the UCB group 71% had progressed to AML and only 48% had achieved CR prior to transplant. This study is thus limited by the heterogeneity of patients/conditioning regimens/supportive care inherent in a registry study and the small number of true MDS patients not progressing to AML receiving an UCB HCT (n = 37).27 Despite these limitations, the analysis importantly highlights surprisingly good outcomes of survival and relapse for such a high-risk group of patients with the majority of the MDS patients progressing to AML, only half in remission, and receiving only RIC. Thus these data suggest that both MUD/UCB RIC transplants can be effective in curing even high-risk MDS/AML patients. Although our study is limited by a relatively small total sample size with shorter follow-up in the UCB cohort, the 44 patients with true MDS undergoing an UCB HCT with an UCB donor source represents the largest published population of such patients to date. The experience at the University of Minnesota developing and fine tuning the approach to UCB transplantation (utilizing UCB in the setting of an urgent transplant need with few unrelated donor options and avoiding use in the setting of extensive marrow fibrosis) along with the

### Table 3. Multivariate analysis: comparison of donor type and MDS disease characteristic risk groups

| Relative risk (95% CI for outcome of interest) | Model with MK | Model with diagnostic R-IPSS cytogenetic risk group |
|----------------------------------------------|--------------|----------------------------------------------------|
| Donor type MK                                | Donor type R-IPSS cytogenetic risk group |
| OS                                           | 1.7          | 1.7  
 | (1.0–3.1)                                   | (1.0–3.1)   |
| DFS                                          | 1.3          | 1.3  
 | (0.8–2.3)                                   | (0.8–2.3)   |
| NRM                                          | 1.7          | 1.7  
 | (0.7–4.1)                                   | (0.8–4.0)   |
| Relapse                                      | 0.7          | 0.8  
 | (0.3–1.5)                                   | (0.4–1.8)   |

Abbreviations: DFS = disease-free survival; MDS = myelodysplastic syndrome; MK = monosomal karyotype; NRM = non-relapse mortality; OS = overall survival; R-IPSS = Revised International Prognostic Scoring System. Sibling is reference for donor type, very low/low is reference for high/very high in CIBMTR MDS HCT (Center for International Bone Marrow Transplant Registry Myelodysplastic Syndrome Transplant) risk group. ‘No’ is reference for monosomal karyotype, very low/low is reference for intermediate/high very high for R-IPSS cytogenetics at diagnosis. Confounding variables for OS and DFS are World Health Organization diagnosis, for relapse are disease status and conditioning. Cells in bold are statistically significant.

### Table 4. COD by donor source

| COD | Siblings (deaths = 25) | UCB (deaths = 24) |
|-----|------------------------|-------------------|
| Graft failure | 0 | 2 (7%) |
| Infection | 6 (24%) | 5 (18%) |
| ARDS | 0 | 1 (4%) |
| aGVHD | 1 (4%) | 2 (7%) |
| cGVHD | 1 (4%) | 0 |
| Disease | 10 (40%) | 9 (32%) |
| Organ failure | 2 (8%) | 3 (11%) |
| New malignancy | 0 | 3 (11%) |
| Hemorrhage | 2 (8%) | 0 |
| Other/unknown | 3 (12%) | 3 (11%) |

Abbreviations: aGVHD = acute GVHD; ARDS = acute respiratory distress syndrome; cGVHD = chronic GVHD; COD = cause of death; UCB = umbilical cord blood.
consistent conditioning platform and supportive care across all patients likely partially explains these differential outcomes between our study and the EBMT-Eurocord analysis.

Predicting outcomes after HCT remains an ongoing area of intense research in MDS. If we can better identify who will do well, or very poorly, with transplant and what prior therapy optimizes disease burden prior to HCT, then we can improve outcomes for patients and eliminate transplant-related risks for those who are unlikely to benefit. Numerous publications have investigated MDS characteristics that may impact HCT outcomes looking at disease burden based on bone marrow blast percentage at the time of transplant,2,3 R-IPSS cytogenetic risk grouping,4 MK and cytogenetic disease burden by percentage of cytogenetically abnormal cells,5 with the general consensus that MK, poor/very-poor R-IPSS cytogenetics, high blast percentage at transplant and high disease burden by percentage of cytogenetically abnormal cells, are adverse predictors of transplant outcomes. Our analysis confirmed the impact of established MDS risk assessments (R-IPSS cytogenetics and MK) on transplant outcomes but small numbers challenge extensive subset analysis.

Relapse was influenced by conditioning intensity with fewer and later relapses in the MA conditioning cohort compared with a higher relapse incidence in the RIC cohort. Interestingly, within the RIC cohort, those not receiving ATG had the highest incidence of relapse. By protocol definition, those who received pre-HCT multi-agent chemotherapy did not require ATG inclusion in the RIC preparative regimen, and thus likely highlights a more advanced MDS patient population. This difference in relapse did not translate into a survival difference between the conditioning intensity cohorts, suggesting that the pace of relapse in MDS disease biology allowed time for additional interventions that prevented death following relapse. Although the recent prospective randomized BMT CTN 0901 trial comparing conditioning intensity in AML and MDS did show increased relapse and a trend toward improved OS in the MA cohort, the study included only a small percentage of MDS patients and thus does not definitively answer the conditioning intensity debate in MDS.29

In summary, our data support the use of UCB donors for MDS patients requiring transplant as a viable alternative donor, highlighting comparable outcomes to sibling donors at an experienced center.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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REFERENCES

1 Sierra J, Perez WS, Rozman C, Carreras E, Klein JP, Rizzo JD et al. Bone marrow transplantation from HLA-identical siblings as treatment for myelodysplasia. Blood 2002; 100: 1997–2004.
2 Warlick ED, Cioc A, Defor T, Dolan M, Weisdorf D. Allogeneic stem cell transplantation for adults with myelodysplastic syndromes: importance of pretransplant disease burden. Biol Blood Marrow Transplant 2009; 15: 30–38.
3 Greenberg P, Cox C, LeBeau MM, Fenaux P, Morel F, Sanz G et al. International scoring system for evaluating prognosis in myelodysplastic syndromes. Blood 1997; 89: 2079–2088.
4 Greenberg PL, Tuechler H, Schanz J, Sanz G, Garcia-Manero G, Soleì F et al. Revised international prognostic scoring system for myelodysplastic syndromes. Blood 2012; 120: 2454–2465.
5 Koreth J, Pidala J, Perez WS, Deeg HJ, Garcia-Manero G, Malcovati L et al. Role of reduced-intensity conditioning allogeneic hematopoietic stem-cell transplantation in older patients with de novo myelodysplastic syndromes: an international collaborative decision analysis. J Clin Oncol 2013; 31: 2662–2670.

6 Cutler CS, Lee SJ, Greenberg P, Deeg HJ, Pérez WS, Anasetti C et al. A decision analysis of allogeneic bone marrow transplantation for the myelodysplastic syndromes: delayed transplantation for low-risk myelodysplasia is associated with improved outcome. Blood 2004; 104: 579–585.
7 Ustun C, Trottier BJ, Sachs Z, DeFor TE, Shune L, Courville EL et al. Monosomal karyotype at the time of diagnosis or transplantation predicts outcomes of allogeneic hematopoietic cell transplantation in myelodysplastic syndrome. Biol Blood Marrow Transplant 2015; 21: 866–872.
8 Della Porta MG, Alessandrino EP, Bacigalupo A, van Lint MT, Malcovati L, Pasculo C et al. Predictive factors for the outcome of allogeneic transplantation in patients with MDS stratified according to the revised IPSS-R. Blood 2014; 123: 2333–2342.
9 Trottier BJ, Sachs Z, DeFor TE, Shune L, Dolan M, Weisdorf DJ et al. Novel disease burden assessment predicts allogeneic transplantation outcomes in myelodysplastic syndrome. Bone Marrow Transplant 2015; 51: 199–204.
10 Saber W, Etzioni RD, Nakamura R, Zhang MJ, Atallah E, Rizzo JD et al. Impact of donor source on hematopoietic cell transplantation outcomes for patients with myelodysplastic syndromes (MDS). Blood 2013; 122: 1974–1982.
11 Lim Z, Brand R, Martino R, van Biesen A, Finke J, Bacigalupo A et al. Allogeneic hematopoietic stem-cell transplantation for patients 50 years or older with myelodysplastic syndromes or secondary acute myeloid leukemia. J Clin Oncol 2010; 28: 405–411.
12 Robin M, Sanz GF, Ionescu I, Rio B, Sirvent A, Renaud M et al. Unrelated cord blood transplantation in adults with myelodysplasia or secondary acute myeloblastic leukemia: a survey on behalf of Eurocord and CLWP of EBMT. Leukemia 2011; 25: 75–81.
13 Vardiman JW, Thiele J, Arbier DA, Brunning RD, Borowitz MJ, Powis A et al. The 2008 revision of the World Health Organization (WHO) classification of myeloid neoplasms and acute leukemia: rationale and important changes. Blood 2009; 114: 937–951.
14 Breems DA, Van Putten WL, De Groot GE, Van Zelderen-Bhola SL, Gersen-Schoor KB, Mellink CH et al. Monosomal karyotype in acute myeloid leukemia: a better indicator of poor prognosis than a complex karyotype. J Clin Oncol 2008; 26: 4791–4797.
15 Brunstein CG, Setubal DC, Wagner JF. Expanding the role of umbilical cord blood transplantation. Br J Haematol 2007; 137: 20–35.
16 Chaplin R, Khouri I, Shimoni A, Gajewski J, Kornblau S, Molldrem J et al. Har-nessing graft-versus-malignancy: non-myeloblastic prophylactic regimens for allogeneic hematopoietic transplantation, an evolving strategy for adoptive immunotherapy. Br J Haematol 2000; 111: 18–29.
17 Bacigalupo A, Ballen K, Rizzo D, Giralt S, Lazarus H, Ho V et al. Defining the intensity of conditioning regimens: working definitions. Biol Blood Marrow Transplant 2009; 15: 1628–1633.
18 Giralt S, Logan B, Rizzo D, Zhang MJ, Ballen K, Emmanouilides C et al. Reduced-intensity conditioning for unrelated donor progenitor cell transplantation: long-term follow-up of the first 285 reported to the national marrow donor program. Biol Blood Marrow Transplant 2007; 13: 844–852.
19 Majhail NS, Brunstein CG, Shanley R, Sandhu K, McClune B, Oran B et al. Reduced-intensity hematopoietic cell transplantation in older patients with AML/MDS: umbilical cord blood is a feasible option for patients without HLA-matched sibling donors. Bone Marrow Transplant 2012; 47: 494–498.
20 Warlick ED, Tomblyn M, Cao Q, Defor T, Blazar BR, Macmillan M et al. Reduced-intensity conditioning followed by related allografts in hematologic malignancies: long-term outcomes most successful in indolent and aggressive non-Hodgkin lymphomas. Biol Blood Marrow Transplant 2011; 17: 1025–1032.
21 Kaplan EL, Meier P. Nonparametric estimation from incomplete observations. J Am Stat Assoc 1958; 53: 457–481.
22 Lin D. Non-parametric inference for cumulative incidence functions in competing risks studies. Stat Med 1997; 16: 901–910.
23 Cox D. Regression models and life tables. J Royal Stat Soc B 1972; 34: 187–220.
24 Fine JP, Gray RJ. A proportional hazards model for the subdistribution of a competing risk. J Am Stat Assoc 1999; 94: 496–509.
25 Colett D. Modelling Survival Data in Medical Research. Chapman & Hall/CRC: London, UK, 2003.
26 Warlick ED, Perfault de Latour R, Shanley R, Robin M, Bejenany N, Xhara A et al. Allogeneic hematopoietic cell transplantation outcomes in acute myeloid leukemia: similar outcomes regardless of donor type. Biol Blood Marrow Transplant 2015; 21: 357–363.
27 Robin M, Ruggeri A, Labopin M, Niedenwieser D, Tabrizi R, Sanz G et al. Comparison of unrelated cord blood and peripheral blood stem cell transplantation in adults with myelodysplastic syndrome after reduced-intensity conditioning regimes: a collaborative study from Eurocord (Cord blood Committee of Cellular Therapy & Immunobiology Working Party of EBMT) and Chronic Malignancies Working Party. Biol Blood Marrow Transplant 2015; 21: 489–495.
28 Deeg HJ, Scott BL, Fang M, Shulman HM, Gyurkocz B, Myerson D et al. Five-group cytogenetic risk classification, monosomal karyotype, and outcome after hematopoietic cell transplantation for MDS or acute leukemia evolving from MDS. Blood 2012; 120: 1398–1408.

29 Scott B, Pasquini M, Logan B, Wu J, Devine S, Porter DL et al. Results of a phase III randomized, multi-center study of allogeneic stem cell transplantation after high versus reduced intensity conditioning in patients with myelodysplastic syndrome (MDS) or acute myeloid leukemia (AML): Blood and Marrow Transplant Clinical Trials Network (BMT CTN) 0901 [abstract]. Blood 2015; 126: LBA-8.