ARTICLE

Outcome of human umbilical cord blood stem cell transplantation (CBT) for acute myeloid leukemia in patients achieving first complete remission after one *versus* two induction courses: a study from the Acute Leukemia Working Party of the European Society for Blood and Marrow Transplantation (EBMT)

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We compared transplantation outcomes of adult patients with AML that underwent cord blood transplantation (CBT) in CR1 following 1 versus 2 induction courses. Study included 325 patients, 243 (75%) with 1 and 82 (25%) with 2 induction courses. Engraftment was lower for patients achieving CR1 after 1 vs. 2 induction courses: 91% vs. 99% ($p = 0.02$). Incidence of acute GVHD was similar, 38% and 36% ($p = 0.81$), as was 2-year chronic GVHD at 23.4% and 27.5%, respectively ($p = 0.65$). Two-year non-relapse mortality (NRM), relapse incidence (RI), leukemia-free survival (LFS), overall survival (OS) and GVHD-free, relapse-free survival (GRFS) were not statistically different between patients achieving CR1 with 1 vs. 2 induction courses with 23% vs. 24% ($p = 0.87$), 25% vs. 30% ($p = 0.4$), 52% vs. 46% ($p = 0.3$), 59% vs. 50% ($p = 0.2$), and 44% vs. 41% ($p = 0.66$), respectively. Results were confirmed by multivariable analysis, NRM (hazard ratio (HR) = 1.1; 95% CI, 0.6–1.8, $p = 0.7$), RI (HR = 1.4; 95% CI, 0.9–2.3, $p = 0.1$), LFS (HR = 1.3; 95% CI, 0.9–1.8, $p = 0.2$), OS (HR = 1.3; 95% CI, 0.9–1.9, $p = 0.1$), and GRFS (HR = 1.1; 95% CI, 0.8–1.5, $p = 0.5$). Overall, outcomes of AML patients undergoing CBT in CR1 achieved after 1 or 2 induction courses are similar.

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INTRODUCTION

Human umbilical cord blood (CB) is an alternative source of hematopoietic cells for patients with acute myeloid leukemia (AML) who are in need of a transplant and lack a human leukocyte antigen (HLA)-compatible sibling or unrelated donor [1–3]. Several factors have been shown to correlate with successful cord blood transplantation (CBT) outcomes including the quality of the umbilical CB based on HLA matching and cell dose as well as the choice of conditioning and anti-graft-versus-host disease (GVHD) prophylaxis [4–6]. Cord blood transplantation (CBT) has been shown to be comparable to transplants with other donor sources establishing CBT as a valuable therapeutic option for patients with AML [7–9].

Furthermore, recent studies have demonstrated favorable hematopoietic stem cell transplantation (HSCT) outcomes in AML patients with detectable measurable residual disease (MRD) at transplantation when offered a CBT [10, 11]. The efficacy of CBT as treatment for AML relies on the immune-mediated graft-versus-leukemia (GVL) effects [12]. In accordance, it was recently demonstrated that CB-derived mismatched HLA class II allele-specific $CD4^+$ T cells recognized primary leukemic cells when the mismatched HLA class II allele was shared between the

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CB unit and the patient, contributing to the CB-mediated GVL effect [13].

Disease status at HSCT, including CBT, is one of the most important prognostic factors for transplantation outcome in AML (1, 4, 11). Results of CBT are usually better in first complete remission (CR1) than in second (CR2) or subsequent complete remission and worst in active disease [7, 11, 14]. Besides disease status, the depth of response assessed as measurable residual disease (MRD) is an important additional factor for CBT outcome [11]. In theory, the pace and rapidity required to achieve leukemic response may impact outcome and overall survival (OS) [15]. We have recently demonstrated that the number of induction courses needed to achieve CR1 is of prognostic significance in AML patients undergoing transplantation from a matched sibling donor (MSD) and a matched unrelated donor (MUD) as well as those undergoing haploidentical transplantation [16, 17]. We compared HSCT outcomes of adults with AML that underwent HSCT in CR1, achieved following 1 or 2 induction courses and demonstrated that 2-year relapse incidence (RI) was higher while leukemia-free survival (LFS), OS and GVHD-free, relapse-free survival (GRFS) were inferior for patients achieving CR1 with 2 vs. 1 course [16, 17]. As CB immunological properties and CBT biology is somewhat different to those of HSCT with bone marrow and peripheral grafts [5, 9, 13] leading to its unique GVL effect [9, 11–13] and advantageous for AML patients with positive pre transplant MRD [10] it may be that in the CBT setting, in contrast to HSCT from MSD, MUD, and haploidentical donors, no difference in transplantation outcome will be observed between patients achieving CR1 after 1 or 2 induction courses. We therefore aimed to compare the outcomes of CBT in AML patients achieving CR after 1 vs. 2 chemotherapy-based induction courses, using the dataset of the Acute Leukemia Working Party (ALWP) of the European Society for Blood and Marrow Transplantation (EBMT) registry.

PATIENTS AND METHODS

Study design and data collection

This was a retrospective, multicenter analysis using the dataset of the ALWP/EBMT (Supplemental material). Eligibility criteria for this analysis included adult patients ≥18 years of age with *de novo* or secondary AML in CR1 after 1 or 2 chemotherapy-based inductions who underwent a first CBT (single or double unit) between 2005 and 2019. The exclusion criteria were HSCT from other donor types (sibling, unrelated or haploidentical donor); previous history of HSCT and disease status >CR1, or unknown before transplantation. Data collected included recipient and donor (cord blood unit) characteristics (age, gender, cytomegalovirus (CMV) serostatus, disease characteristics, number of induction chemotherapy courses, disease status at transplant, year of transplant, type of conditioning regimen, stem cell source, and GVHD prophylaxis regimen. Pre-transplantation MRD status and allocation to MRD-negative or MRD-positive groups were determined by individual participating centers and utilized molecular and/or immunophenotyping criteria methodology [18]. The conditioning regimen was defined as myeloablative (MAC) or reduced intensity (RIC) based on the reports from individual transplant centers as per previously established criteria [19]. The conditioning regimen was defined as MAC when containing total body irradiation (TBI) with a dose >6 Gray or a total dose of busulfan (Bu) >8 mg/kg or >6.4 mg/kg when administered orally or intravenously, respectively. All other regimens were defined as RIC [19]. Regimens for GVHD prophylaxis were per institutional protocols. Grading of acute (a) GVHD was performed using established criteria [20]. Chronic (c) GVHD was classified as limited or extensive according to published criteria [21]. For this study, all necessary data were collected according to the EBMT guidelines, using the EBMT minimum essential data forms. The list of institutions contributing data to this study is provided in the Supplementary Appendix.

Statistical analysis

The study endpoints were OS, LFS, RI, NRM, engraftment, aGVHD, cGVHD, and GRFS. All endpoints were measured from the time of transplantation. Engraftment was defined as achieving an absolute neutrophil count of 0.5×10^9/L for three consecutive days. OS was defined as time to death from any cause. LFS was defined as survival with no evidence of relapse or progression. NRM was defined as death from any cause without previous relapse or progression. We used modified GRFS criteria. GRFS events were defined as the first event among grade III–IV aGVHD, extensive cGVHD, relapse, or death from any other cause [22]. Median values and ranges were used for continuous variables and frequencies and percentages for categorical variables [23]. Patient, disease, and transplant-related characteristics were compared between the two groups (1 vs. 2 induction courses) using the Mann–Whitney *U* test for numerical variables, and the chi-squared or Fisher's exact test for categorical variables. The probabilities of OS, LFS, and GRFS were calculated using the Kaplan–Meier (KM) estimate. The RI and NRM were calculated using cumulative incidence (CI) curves in a competing risk setting, death in remission being treated as a competing event for relapse. Death was considered as a competing event for engraftment. To estimate the CI of acute or cGVHD, relapse and death were considered as competing events. Univariate analyses were performed using the log-rank test for LFS, OS, and GRFS while Gray's test was used for CI. Multivariate analyses were performed using the Cox proportional-hazards regression model. Variables included in the multivariate model were age, cytogenetics (adverse vs. other), double vs. single CB unit, patient CMV status, in vivo T-cell depletion (TCD), and conditioning intensity (MAC vs. RIC). To test for a center effect, we introduced a random effect or frailty for each Center into the model [24]. Results were expressed as the hazard ratio (HR) with a 95% confidence interval (95% CI). All *p* values were two-sided with a type 1 error rate fixed at 0.05. Statistical analyses were performed with SPSS 25.0 (SPSS Inc., Chicago, IL, USA) and R 4.0.2 [25].

RESULTS

Patient, transplant, and disease characteristics

A total of 325 patients met the inclusion criteria, 243 (75%) with 1, and 82 (25%) with 2 induction chemotherapy courses. Table 1 shows the baseline demographic and clinical characteristics. Time from diagnosis to CR in the 2 induction group was almost double that of the 1 induction group patients, being 76 (interquartile range [IQR], 58–93) vs. 43 (IQR, 36–54) days vs. days ($p < 0.0001$), while time from CR to CBT was 80 (IQR, 49–138) vs. 112 (IQR, 86–154) days ($p < 0.0001$), for 1 vs. 2 induction courses, respectively (Table 1). All patients were at CR1 at time of HSCT. One hundred and six (44%) patients and 29 (35%) patients in the 1 vs. 2 induction groups, respectively, were transplanted with 1 CB unit while 137 (56%) and 53 (64%), respectively, received 2 CB units (Table 2). The median cell counts were 0.39×10^{10} (IQR, 0.24–0.57) for total nucleated cells (TNC) and 0.12×10^8 (IQR, 0.05–0.24) for $CD34^+$ cells vs. 0.39×10^{10} (IQR, 0.25–0.53) and 0.11×10^8 (IQR, 0.05–0.24) in patients receiving 1 vs. 2 induction courses, respectively, p = NS. Conditioning was MAC in 43% and 37% and reduced intensity (RIC) in 57% and 63%, respectively ($p = 0.31$) (Table 2). The most frequent conditioning was fludarabine (Flu)/busulfan (Bu) based for 31% and 18% for patients receiving 1 vs. 2 induction courses, respectively ($p = 0.086$) (Table 2). Sixty-two percent and 76% of the patients received total body irradiation (TBI), respectively (Table 2). The most frequent anti-GVHD prophylaxis was cyclosporine A (CSA) and mycophenolate mofetil (MMF) in 76% and 83%, or CSA (with or without steroids) in 16 % and 11%, respectively. Anti-thymocyte globulin (ATG) was administered to 33% and 26% of the CBT recipients, respectively ($p = 0.22$) (Table 2).

Transplantation outcomes

Cumulative incidence of absolute neutrophil count (ANC) ≥ 0.5×10^9/L was lower for patients achieving CR1 after 1 vs. 2 induction courses: 91% vs. 99% of the patients ($p = 0.02$).

Day 180 incidence of acute GVHD (aGVHD) grades II–IV was similar in both induction groups, 38% (33–43%) and 36% (26–48%) ($p = 0.81$), as was grades III–IV 12% (8–17%) and 9% (4–17%) ($p = 0.41$), respectively (Table 3). Two-year total chronic GVHD was 23% (18–29%) and 27% (18–38%), respectively

Table 1. Patient and disease characteristics.

Clinical parameter	1 Induction ($n = 243$)	2 Inductions ($n = 82$)	P
Follow-up (months), median [95% CI]	65.4 [57.4–73.5]	51.0 [34.8–61.5]	0.62
Patient age (years), median (min–max) [IQR]	49.4 (19–70.9) [35.6–60]	52.1 (19.2–71.5) [36.8–59.7]	0.84
Patient sex			
Male	120 (49.4%)	47 (57.3%)	0.21
Female	123 (50.6%)	35 (42.7%)	
Diagnosis			
De novo	225 (92.6%)	78 (95.1%)	0.61
SecAML	18 (7.4%)	4 (4.9%)	
Cytogenetics			
Favorable	11 (4.5%)	1 (1.2%)	0.046
Interm	142 (58.4%)	61 (74.4%)	
Adverse	76 (31.3%)	15 (18.3%)	
NA/failed	14 (5.8%)	5 (6.1%)	
FLT3-ITD			
FLT3 neg	120 (66.3%)	42 (67.7%)	0.84
FLT3 pos	61 (33.7%)	20 (32.3%)	
Donor sex			
Donor male	113 (49.1%)	40 (50.6%)	0.82
Donor female	117 (50.9%)	39 (49.4%)	
Karnofsky score			
<90	55 (25.3%)	20 (29%)	0.55
≥90	162 (74.7%)	49 (71%)	
Missing	26	13	
Patient CMV			
Pat. CMV neg.	101 (42.1%)	37 (45.1%)	0.63
Pat. CMV pos	139 (57.9%)	45 (54.9%)	
Missing	3	0	

CR1 first complete remission, *IQR* interquartile range, *CBT* cord blood transplantation, *Sec* secondary, *AML* acute myelogenous leukemia, *interm* intermediate, *Sec* secondary, *NA* not available, *FLT3-ITD* FMS-like tyrosine kinase 3 internal tandem duplication mutation, *Pat* patient, *CMV* cytomegalovirus, *neg* negative, *pos* positive.

Table 2. Transplant characteristics.

Clinical parameter	1 Induction ($n = 243$)	2 Inductions ($n = 82$)	P
Conditioning regimen intensity			
MAC	104 (43%)	30 (36.6%)	0.31
RIC	138 (57%)	52 (63.4%)	
Conditioning regimen			
BuCy ± other	10 (4.1%)	4 (4.9%)	0.086
BuFlu ± other	75 (31%)	15 (18.3%)	
TBI ± other	149 (61.6%)	62 (75.6%)	
OtherCT	8 (3.3%)	1 (1.2%)	
GVHD prophylaxis			
Csa	39 (16.1%)	9 (11.2%)	
Csa + mtx	6 (2.5%)	2 (2.5%)	
Csa + mmf	183 (75.6%)	66 (82.5%)	
In vivo T-cell depletion			
No ATG	163 (67.1%)	61 (74.4%)	0.22
ATG	80 (32.9%)	21 (25.6%)	

MAC myeloablative conditioning, *RIC* reduced intensity conditioning, *Bu* busulfan, *Cy* cytoxan, *Flu* fludarabine, *CT* chemotherapy, *TBI* total body irradiation, *GVHD* graft-versus-host disease, *Csa* cyclosporine A, *mtx* methotrexate, *mmf* mycophenolate mofetil, *TCD* T-cell depletion, *ATG* anti-thymocyte globulin.

Table 3. Transplantation outcome.

Clinical parameter	1 Induction ($n = 243$)	2 Inductions ($n = 82$)	P
Engraftment HSCT			
Engrafted	221 (91.3%)	81 (98.8%)	
Graft failure	21 (8.7%)	1 (1.2%)	0.02
Missing	1	0	
Acute GVHD			
Grade I	30 (12.4%)	13 (16%)	NA
Grade II	62 (25.7%)	22 (27.2%)	
Grade III	21 (8.7%)	3 (3.7%)	
Grade IV	9 (3.7%)	4 (4.9%)	
Present, grade unknown	4 (1.7%)	3 (3.7%)	
No aGvHD present (Grade 0)	115 (47.7%)	36 (44.4%)	
Missing	2	1	

HSCT hematopoietic stem cell transplantation, *GVHD* graft-versus-host disease, *a* acute, *NA* not available.

($p = 0.65$). In univariate analysis, the 2-year NRM, RI, LFS, OS and GRFS were not significantly different between patients achieving CR1 with 1 vs. 2 induction courses with 23% (17–28%) vs. 24% (15–33%) ($p = 0.87$), 25% (20–31%) vs. 30% (20–41%) ($p = 0.39$), 52% (46–59%) vs. 46% (35–59%) ($p = 0.33$), 59% (52–65%) vs. 50% (38–61%) ($p = 0.22$), and 44% (37–50%) vs. 41% (30–52%) ($p = 0.66$), respectively, Fig. 1.

Cause of death

A total of 114 (47%) and 44 (54%) patients in the 1 and 2 induction cohorts, respectively, died during the study period. Disease relapse, infection and GVHD-related death was the most common cause of death in both groups (Table 4). Other causes were infrequent and included deaths due to multiorgan failure (MOF), second malignancies, central nervous system (CNS) toxicity, and hemorrhage (Table 4).

Multivariate analysis

These results were confirmed in the MVA (Supplemental Table 1). There was no significant association between 2 vs. 1 induction course groups and CBT outcome: NRM (hazard ratio (HR) = 1.1; 95% CI, 0.65–1.84, p = 0.73), RI (HR = 1.43; 95% CI, 0.91–2.26, $p = 0.12$), LFS (HR = 1.27; 95% CI, 0.91–1.79, $p = 0.16$), OS (HR = 1.32; 95% CI, 0.92–1.88, $p = 0.13$), and GRFS (HR = 1.1; 95% CI, 0.8–1.52, $p = 0.55$) (Supplemental Table 1). Risk of aGVHD grade II–IV and cGVHD did not differ significantly with a HR = 0.9 (0.59–1.38, $p = 0.63$) and HR = 1.18 (0.7–1.98, $p = 0.53$), respectively. Other significant prognostic factors in the MVA for CBT outcome parameters were non adverse cytogenetics for lower RI, HR = 0.45 (95% CI, 0.29–0.68, $p = 0.0002$) and higher LFS, HR = 0.67 (95% CI, 0.48–0.92, $p = 0.015$). TCD was associated with lower risk of aGVHD, HR = 0.39 (95% CI, 0.23–0.66, $p = 0.0005$) but higher NRM, HR = 1.99 (95% CI, 1.14–3.49, $p = 0.016$) leading to worse OS, HR = 1.53(95% CI, 1.02–2.29, $p = 0.042$). RIC was associated with lower

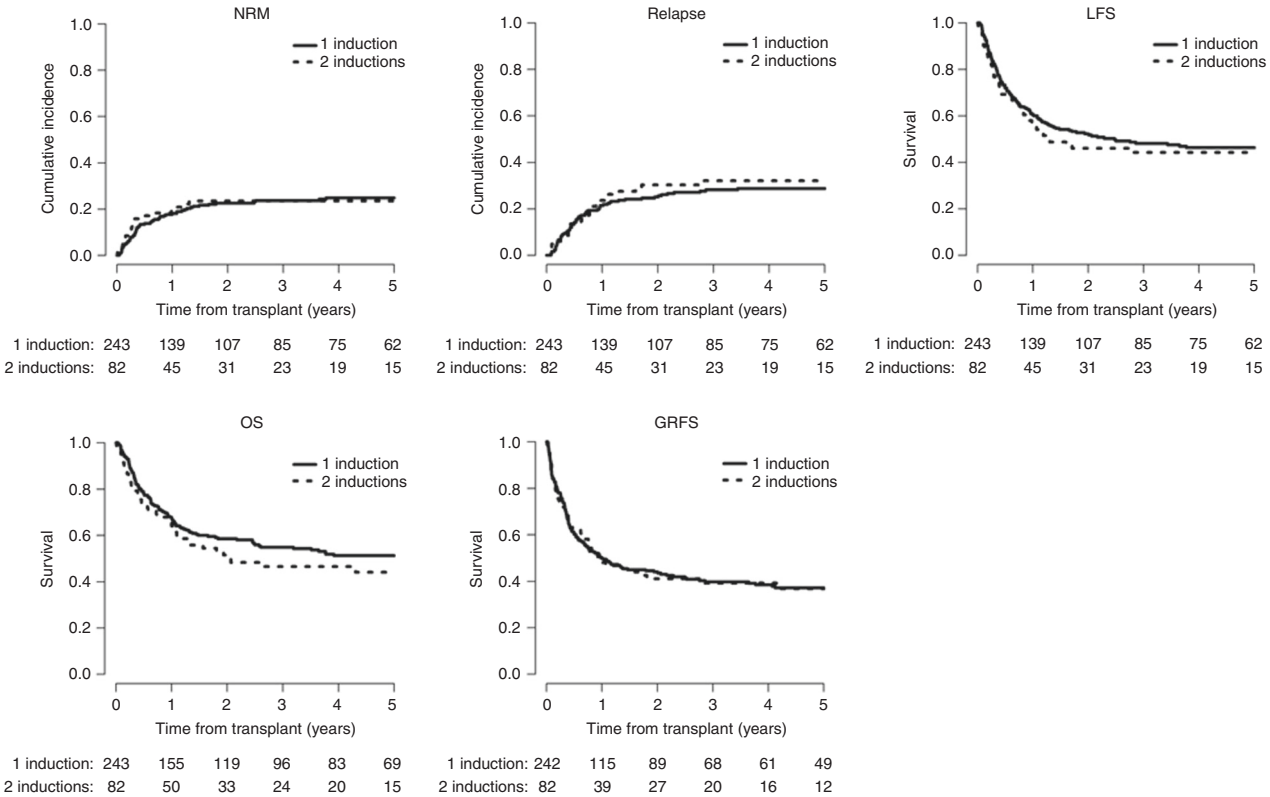

Fig. 1 Transplantation outcome of human umbilical cord blood stem cell transplantation (CBT) for patients with acute myeloid leukemia achieving first complete remission after one versus two induction courses. Non-relapse mortality (NRM), relapse incidence (RI), leukemia-free survival (LFS), overall survival (OS) and GVHD-free, relapse-free survival (GRFS).

Table 4. Cause of death.

Clinical parameter	1 Induction ($n = 114$)	2 Inductions ($n = 44$)
Haemorrhage	2 (1.8%)	0 (0%)
Infection	30 (26.5%)	7 (15.9%)
GVHD	16 (14.2%)	7 (15.9%)
Original disease	51 (45.1%)	24 (54.5%)
Other second malignancy	2 (1.8%)	1 (2.3%)
MOF	3 (2.7%)	1 (2.3%)
CNS toxicity	4 (3.5%)	1 (2.3%)
Other transp related	1 (0.9%)	0 (0%)
Other not HSCT related	4 (3.5%)	3 (6.8%)
Missing	1	0

GVHD acute graft-versus-host disease, *MOF* multiorgan failure, *CNS* central nervous system, *transp* transplant, HSCT hematopoietic stem cell transplantation.

risk of aGVHD, HR = 0.58(95% CI, 0.36–0.94, $p = 0.026$). Patient CMV seropositivity was a borderline risk factor for lower GRFS, HR = 1.34 (95% CI, 1–1.81, $p = 0.05$). Of note, no difference was observed in transplantation outcome between patients transplanted with single vs. double CB units (Supplemental Table 1).

DISCUSSION

In the current study we observed that in AML patients undergoing CBT in CR, besides engraftment, all other transplantation outcome parameters including NRM, RI, LFS, OS, and GRFS did not differ between patients achieving CR after 1 vs. 2 induction courses. These findings are in contrast to previous publications that have indicated better outcomes in AML patients achieving CR after 1 induction chemotherapy course in comparison to those needing >1 course. For example, a previous non-transplant study by the UK National Cancer Research Institute (NCRI) reported that the 5-year survival was significantly better in patients that attained CR after the first induction course vs. those that attained CR only after the second course, 40% vs. 23%, respectively ($p = 0.0008$) [26]. We recently performed a retrospective analysis of 302 consecutive AML patients treated with intensive induction chemotherapy at our institution between 2007 and 2020. Sixty percent of the patients attained remission following initial chemotherapy while 20% required an additional cycle of intensive chemotherapy for remission. On MVA achievement of remission following 2 cycles of intensive chemotherapy compared with a single cycle resulted in significantly inferior survival (HR = 1.67, 95% CI, 1.07–2.59; $p = 0.025$) [16]. Similarly, in the transplant setting, Lim et al. compared transplantation outcome in 45 patients with high-risk AML achieving CR after 1–2 inductions vs. 3 or more inductions pre-HSCT from MSD or unrelated donors and demonstrated a trend toward better progression-free survival and OS in the former [27]. Walter et al. performed a similar study in 220 AML patients following HLA-matched transplantation and demonstrated that patients who required 2 induction courses to achieve CR had shorter relapse-free survival and increased RI relative to those who required only 1 induction course to achieve CR [28]. We recently compared transplantation outcomes of 635 AML patients who underwent haploidentical HSCT (HaploSCT) in CR1, achieved following 1 (74% of the patients) or 2 (26% of the patients) induction courses. HaploSCT outcome was superior in AML patients achieving CR after 1 course of induction chemotherapy

compared to those that required 2 courses, with a lower relapse rate and better LFS, OS and GRFS [17]. We envisage that the observed worse results in AML patients needing a higher cumulative dose of chemotherapy (2 courses) to achieve a CR may speak of a more malignant leukemic disease and this may be a surrogate marker for leukemic resistance. The current finding that in the setting of CBT, no difference could be observed between AML patients that did and did not achieve a CR post 1 course of induction chemotherapy may indicate that the unique immunological properties of CB and the CBT-mediated GVL effect may substitute for the traditional need for additional chemotherapy in the former group of AML patients in order to mediate an effective anti-leukemic effect, ensuring a successful transplantation outcome. As for GVL effects post CBT, Baron et al. demonstrated recently that the GVL effects are the main mechanisms protecting against late relapse after CBT as the conditioning intensity impacted the risk of relapse only during the first 18 months after CBT but had no impact thereafter [12]. In another study, comparing transplantation outcome following HSCT from MSD, unrelated, and haploidentical donors as well as CB, using the Seattle non-MAC regimens, the authors demonstrated that the intensity of GVL effects was comparable with these four transplant approaches with a similar GVL effect in single unit vs. double unit CBT and that after day 100, CBT was associated with a significantly better GRFS [9]. Additional support for the effective GVL post CBT was reported by Lamers et al. who provided information to suggest that a $CD4^+$ T cell-mediated graft-versus-graft alloreactivity potentially adds to and facilitates the GVL effect in the CBT setting and especially after double unit CBT [13]. The only difference in CBT outcome parameters that we observed between patients achieving CR after 1 vs. 2 induction courses was lower engraftment rates for patients achieving CR1 after 1 vs. 2 induction courses which may indicate that the additional chemotherapy administrated to the patients that received 2 induction courses was of biological significance and contributed to the hematopoietic stem cell engraftment.

Adverse cytogenetics was a prognostic factor in our study for RI and LFS as has been previously reported [29, 30]. Also, confirming previously published results, we observed comparable RI, LFS, and OS in patients given single vs. double CBT [31, 32] (and no impact of conditioning intensity on OS although RIC regimen was associated with a lower risk of aGVHD) [6]. This study also confirms that although the use of TCD was associated with lower aGVHD incidence it was also associated with higher NRM and lower OS [4]. This most probably reflects the negative impact of high ATG exposure on immune reconstitution and infection risk in the umbilical CBT setting [33]. Finally, patient CMV seropositivity was a borderline risk for GVHD in accordance with previous publications [4, 6].

This being a retrospective, registry-based transplantation study, there are several limitations including the possibility of unavailable data that have not been considered, such as molecular and MRD data as well as cord blood cell dose and HLA disparity characteristics, not being available for a large proportion of patients. Moreover, as we lacked pre-transplantation data, we cannot exclude confounding due to unmeasured factors. Finally, the landscape of treating AML is changing and more and more AML patients are receiving novel compounds like azacitidine and decitabine with or without venetoclax or Vyxeos (CPX-351) and our findings are applicable only to AML patients receiving the traditional $7+3$ induction regimen [34]. Furthermore, recent advances in the field of CBT expansion might solve the problem of graft failure following CBT [35, 36]. In conclusion, in this relatively large registry-based, retrospective analysis, patients with AML undergoing CBT in CR1 following 1 or 2 induction courses had similar outcomes which may indicate a GVL effect post CBT.

DATA AVAILABILITY

AN, ML, and MM had full access to all study data (available upon data-specific request).

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AUTHOR CONTRIBUTIONS

AN wrote the manuscript, designed the study, and interpreted the data. ML designed the study, performed the statistical analyses, interpreted the data, and edited the manuscript. MM, ML, AR, and FB designed the study, interpreted the data, and edited the manuscript. JJC, EF, PC, NF, JS, DD, HLW, JLB, AN and DB reviewed the manuscript and provided clinical data. All authors approved the final version of the manuscript.

COMPETING INTERESTS

The authors declare no competing interests.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

The scientific boards of the ALWP of the EBMT approved this study.

ADDITIONAL INFORMATION

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