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A novel clofarabine bridge strategy facilitates allogeneic transplantation in patients with relapsed/refractory leukemia and high-risk myelodysplastic syndromes

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Abstract

Patients with relapsed/refractory leukemias or advanced myelodysplastic syndrome (MDS) fare poorly following allogeneic hematopoietic cell transplant (HCT). We report prospective phase II study results of 29 patients given clofarabine 30 mg/m^2/day i.v. × 5 days followed immediately by HCT conditioning while at the cytopenic nadir. A total of 15/29 patients (52%) were cytoreduced according to pre-defined criteria (cellularity < 20% and blasts < 10%). Marrow cellularity (P < 0.0001) and blast% (P = 0.03) were reduced. Toxicities were acceptable, with transient hyperbilirubinemia (48%) and gr3–4 infections (10%). In all, 28/29 proceeded to transplant; 27 received ATG or alemtuzumab. Post HCT, 180 day non-relapse mortality (NRM) was 7% (95% confidence interval (CI): 1–21), relapse was 29% (95% CI: 13–46) and OS was 71% (95% CI: 51–

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CONFLICT OF INTEREST

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85), comparing favorably to published data for high-risk patients. Two-year graft vs host disease incidence was 40% (95% CI: 21–58) and 2 year OS was 31% (95% CI: 14–48). Disease at the nadir correlated with inferior OS after HCT (HR = 1.22 for each 10% marrow blasts, 95% CI: 1.02–1.46). For AML/MDS patients, there was a suggestion that successful cytoreduction increased PFS (330 vs 171 days, $P = 0.3$) and OS (375 vs 195 days, $P = 0.31$). Clofarabine used as a bridge to HCT reduces disease burden, is well tolerated, and permits high-risk patients to undergo HCT with acceptable NRM. Late relapses are common; thus, additional strategies should be pursued. NCT-00724009.

Keywords

allo-SCT; relapsed leukemia; AML; bridge therapy; myelodysplastic syndrome

INTRODUCTION

Allogeneic hematopoietic SCT (HCT) offers a curative approach to patients with high-risk or refractory AML, ALL, CML or myelodysplastic syndrome (MDS). Leukemia patients with primary refractory disease or uncontrolled relapse have a very poor prognosis,[1] and those with active disease at HCT fare poorly regardless of regimen intensity.[2,3] Relapsed/refractory patients typically receive multiple lines of salvage therapy in an attempt to achieve remission, because greater disease burden strongly predicts for poor outcomes after HCT.[2–7] This approach leads to increased toxicity and may allow disease evolution, further compromising the opportunity to undergo HCT. Induction therapy followed immediately by transplant conditioning while still at the cytopenic nadir may circumvent these problems.[8,9]

Clofarabine, a purine nucleoside with activity against AML and MDS, is well tolerated in adults with the most common side effects being hematological toxicity, transient transaminitis and creatinine elevation.[10–12] Recently, clofarabine was safely incorporated into HCT conditioning regimens with particular success in patients with active myeloid malignancies.[13–16]

We previously reported a retrospective review of the safety of initiating HCT conditioning during the hematological nadir following clofarabine induction. Importantly, clofarabine extrame-dullary toxicities were non-overlapping with those of conditioning regimens and patients were able to proceed to transplant.[17] Based upon these observations we designed a prospective study of clofarabine induction followed by transplant conditioning for relapsed/refractory leukemia and MDS patients, to test the feasibility of proceeding to transplant and reducing disease burden.

MATERIALS AND METHODS

This IRB approved feasibility study took place at the University of Chicago Medical Center (ClinicalTrials.govIdentifier: NCT-00724009). Enrollment was from March 2008 to September 2010.

Study objectives

The primary endpoint was achievement of cytoreductive response, defined as a nadir (day 12 following initiation of clofarabine) BM biopsy with a cellularity of < 20% and a blasts < 10% of all cellular elements before initiation of HCT conditioning.[17,18] To maintain uniformity, one hematopathologist reviewed all cases.

Secondary endpoints included day 100, day 180 and 1 year OS, PFS, non-relapse mortality (NRM), relapse rate; clofarabine toxicity; proportion proceeding to HCT; and whether BM cellularity and blast % after clofarabine predicts PFS or OS after HCT.

Patient eligibility

Patients with relapsed/refractory AML or ALL, MDS with >5% BM myeloblasts, or CML in accelerated or blast phase or resistant/intolerant to imatinib, dasatinib and/or nilotinib were eligible. All patients had an identified matched related donor, matched unrelated donor, mismatched unrelated donor or suitable cord blood donor unit and were otherwise eligible and cleared, per institutional guidelines, to proceed to transplant. Peripheral blood progenitor cells were preferred using G-CSF mobilization. HLA matching was performed at HLA-A, HLA-B, HLA-C and HLA-DRB1 by high-resolution techniques. Criteria for cord blood matching followed standard criteria: low-resolution at HLA-A, and HLA-B and high-resolution at HLA-DRB1.

Eligibility required serum glutamic oxaloacetic transaminase (SGOT)/ serum glutamic pyruvic transaminase ≤2.5 × upper limit normal; alkaline phosphatase ≤2.5 × upper limit normal; serum bilirubin < 1.5 mg/dL; serum creatinine < 1.0 mg/dL or creatinine clearance > 60 mL/min; age≥/ = 18 years; ECOG performance status ≤/ = 2.[19] All patients provided informed written consent.

Treatment schema

Clofarabine 30 mg/m^2 was i.v. administered consecutively for 5 days, with dexamethasone 10mg i.v. administered 1.5 h before clofarabine. HCT conditioning was to begin at the hematological nadir, 12–21 days after clofarabine initiation (Figure 1). Conditioning regimens and GVHD prophylaxis for each patient were at the discretion of the treating physician in accordance with institutional guidelines based upon disease, patient and donor characteristics and were not dependent upon response or toxicity to clofarabine cytoreduction.[15,20–23] Continuation to HCT after clofarabine was at the discretion of the treating physician. Post-transplant immunosuppression was tacrolimus from day −2 to day + 100 for matched related donor recipients and until day + 180 for unrelated adult donor recipients. For cord blood recipients, tacrolimus was from day −1 to day + 180 and mycophenolate mofetil from day − 3 to day + 56. The majority of patients received either ATG or alemtuzumab.

Study monitoring and statistical design

Based upon our retrospective data we hypothesized that 66% of patients would achieve a cytoreductive response, defined as a post clofarabine BM biopsy with < 20% cellularity and < 10% blasts,[17] and an unacceptable result would be if only 40% achieved this. The one

stage design required 27 patients to test the null hypothesis that the response is ≤40% against the alternative that it is ≥ 60% for a one-sided α of 0.10 and 90% power. To account for cumulative toxicity of clofarabine in conjunction with the HCT regimen, we utilized a toxicity monitoring plan based on Pocock-type boundaries.[24] For this stopping threshold, we counted ≥Grade 3 toxicities preventing cell infusion within 30 days after clofarabine. Unacceptable toxicity was defined as 25% by day 30.

Secondary endpoints included analysis of the AML/MDS subset. Kaplan–Meier curves for PFS and OS were generated. Cumulative incidence curves for relapse, NRM and GVHD were generated. NRM was defined as death from any cause without evidence of relapse. Time to event analysis used the day of transplant as day 0. Patients were stratified by cytoreduced or non-cytoreduced and outcomes compared using Wilcoxon-test statistic. Toxicity associated with clofarabine was assessed prospectively using CTCAE v.3. Descriptive statistics were used for other endpoints. Complete donor chimerism was defined as > 95% donor cells in both the unfractionated and CD3 compartments as evaluated by variable number of tandem repeats methodology. Cytogenetics for AML patients at diagnosis were classified according to CALGB criteria.[25]

RESULTS

Patient characteristics

Twenty nine patients were enrolled. Patient characteristics are presented in Table 1. Only two did not meet high-risk CIBMTR classification: one had tyrosine kinase inhibitor resistant Ph + CML in CP1 with loss of cytogenetic response to imatinib, and failure to respond to nilotonib and dasatinib; the other had CML in CP2 with prior progression to blast phase while on imatinib and failed to respond to dasatinib. Patients were heavily pretreated and often refractory to prior therapy. No MDS patient treated with a hypomethylating agent responded (n = 6). Another MDS patient failed a lenalidomide-based regimen. All AML patients were relapsed or refractory. All AML patients received ara-C as part of their induction regimen. For the seven AML patients that previously achieved CR1 (n = 7), the median duration was 1 month (range < 1– 15 months) with the remaining 9 having primary induction failure. AML patients that achieved CR1 recieved high-dose ara-C consolidation. Salvage therapy containing ara-C was given to 10 AML patients at relapse or after failed standard 7 + 3 ara-C and anthracycline induction. Only two AML patients had achieved a CR1 > 12 months and both were transplanted in CR1 (1 auto and 1 allo). Myeloproliferative disorder patients included a JAK2 mutated primary myelofibrosis in accelerated phase managed only with corticosteroids before transplant.

Cytoreduction and feasibility of transplant

Transplant characteristics are presented in Table 1. RIC was used in the majority of patients (25/29, 86%) and most received PBSC allografts (22/29, 76%).

A cytoreductive response was achieved in 15/29 patients (52%), and 13/24 (54%) patients in the MDS/AML subset.[17] BM cellularity and blast percentage before and after clofarabine

are presented in Figure 2. Circulating blasts were present in 18/29 (62%) patients at the time of clofarabine and 7/29 patients (24%) at the time of conditioning.

Twenty eight of 29 patients received an allogeneic transplant. One patient had conditioning initiated after cytoreduction, but died of sepsis before stem cell infusion. Conditioning was initiated at the nadir after one cycle of clofarabine for 26/28 patients: one patient developed infection necessitating delay and another had progressive disease. Both patients went on to receive HiDAC + mitoxantrone cytoreduction and underwent transplantation at the nadir.

Toxicity of clofarabine bridge and conditioning regimen

Toxicities are summarized in Table 2. SGOT and total bilirubin elevations were common but transient: all patients had normal total bilirubin on HCT day 0. Relative to clofarabine the median peak SGOT elevation was day 5 (range 3–31) and peak bilirubin was day 8 (range 2–31). There were no cases of veno-occlusive disease. Three patients developed neutropenia-associated infection following clofarabine but before conditioning: one aspergillus pneumonia responded to treatment and the patient was transplanted after delay; another developed a tunneled catheter infection requiring debridement; a third patient developed genital HSV, which responded to therapy. Nine patients had grade 3 or 4 infection after the start of conditioning therapy but before day + 12 after HCT. One patient with refractory AML underwent conditioning but died 1 day before stem cell infusion due to sepsis (grade 5 infection).

Transplant outcomes

Median days to engraftment were 11 (95% confidence interval (CI): 10–12) for neutrophils and 22 (95% CI: 18–35) for platelets. At day 30 after transplant, 27/28 patients remained alive. One patient relapsed on day + 28, the remaining 26 patients had morphological CR by day + 30 BM biopsy. Of these 26, 25 had an evaluable BM cytogenetic samples showing reemergence of a normal karyotype.[25] Day + 30 chimerism results for patients in remission were: 100% (n = 26) unsorted complete donor chimerism and 88% (n = 23) CD3 complete donor chimerism.

Three HCT patients died before day 100; one in remission from sepsis and two of progressive disease. The 100 day cumulative incidence of NRM was 3.6%. For all patients receiving clofarabine, 2/29 died in remission before HCT day + 100.

The 100 day, 6-month and 1-year cumulative incidence of grade 2–4 acute GVHD were 21% (95% CI: 9–38), 29% (95% CI: 13–46) and 35% (95% CI: 18–54). There were no cases of grade 3–4 acute GVHD before day 100. Two late onset acute GVHD cases occurred after day 100, making the 100 day, 6-month and 1-year cumulative incidence of grade 3–4 acute GVHD were 0%, 4% (95% CI: 0–16) and 7% (95% CI: 1–21). The cumulative incidence of chronic GVHD was 7% (95% CI: 1–21%) at 1 year and 7% (95% CI: 1–21) at 2 years. Of the three patients with chronic GVHD, two were mild and one moderate by NIH consensus criteria.

Survival analysis

With a median follow-up of 854 days after HCT for 9 survivors, median PFS was 211 days (95% CI: 171–342) and median OS was 332 days (95% CI: 195–629) (Figure 3). For AML and MDS patients (n = 23), median PFS was 251 days (95% CI: 173–358) and median OS was 373 days (95% CI: > 220). The median days to relapse, by competing risk analysis, were 330 days (95% CI: 173–599) for all patients, and 330 days (95% CI: 187–599) for AML/MDS patients. Outcomes at day 100, 6 months and 1 year are summarized in Table 3. The Kaplan–Meier estimate for two OS was 31% (95% CI: 14– 48) for all patients and 33% (95% CI: 14–52) for AML/MDS patients.

Median PFS for cytoreduced patients compared with those not achieving cytoreduction was 251 (range 27–1433) vs 171 days (range 27–916) (P = 0.4); median OS was 360 (range 27–1433) vs 195 (range 90–916) days (P = 0.4). Subset analysis of AML and MDS patients revealed median PFS for cytoreduced vs non-cytoreduced patients was 330 (range 116–1433) vs 171 (range 27–897) days (P = 0.3) and median OS was 375 (range 137–1433) vs 195 (range 90–897) days (P = 0.31).

Prognostic factors

The pre-clofarabine BM blast percentage did not predict post-transplant OS (HR = 0.9, 95% CI: 0.74–1.09). Each 10% increase in blasts present in the post clofarabine BM biopsy was associated with decreased OS following transplant (HR = 1.22, 95% CI: 1.02– 1.46). The following factors: age > 50 years; poor-risk cytogenetics; and circulating blasts, did not predict achievement of cytoreduction, OS or PFS in the entire cohort or the AML/MDS subset. Lack of an HLA-matched related donor did not predict for OS or PFS.

DISCUSSION

This trial demonstrates that clofarabine induction 2 weeks before initiation of transplant conditioning is a tolerable and effective bridge strategy allowing allogeneic HCT in those patients with persistent disease. The majority of all patients (52%), and the AML/ MDS subset (54%), achieved the primary endpoint of cytoreduction.[17] Clofarabine reduced marrow blast% (P = 0.03) and cellularity (P < 0.0001). All patients proceeded to conditioning, with only one death before allograft infusion and one non-relapse death before day + 100.

The lack of cytoreduction in a substantial minority may relate to highly resistant disease and/or insufficient clofarabine dose intensity. Clofarabine has efficacy against AML at 40 mg/m^2 daily × 5. The dose in this trial was 30 mg/m^2 daily × 5 based on studies showing the lower dose has activity in older adults with AML.[11] These cytoreduction results are consistent with published overall response rates of 47% for clofarabine + cytarabine compared with 23% for cytarabine + placebo induction for relapsed/refractory AML.[26]

Renal, skin and cardiac toxicities attributable to clofarabine were minimal and acceptable. Transaminase and bilirubin elevations were common yet transient: all patients had a normal bilirubin, and 4% had grade 3–4 SGOT elevation on the day of transplant. No patients

developed veno-occlusive disease. The majority received T-cell depletion, which likely contributed to tolerability by minimizing early acute GVHD.

Successful cytoreduction did not clearly improve clinical outcomes and the results do not support a practice of canceling transplant if cytoreduction is not achieved as the study was not powered to show clinical differences. However, there was quantitatively better survival (with wide CIs) for patients successfully cytoreduced, particularly in the MDS/AML subset.

Our study is limited in the ability to make definitive recommendations for a number of reasons including the small sample size, patient and disease heterogeneity, and variability in transplant characteristics. The inclusion of ALL and CML patients weakens conclusions surrounding cytoreduction and clinical outcomes, as the efficacy of clofarabine for treatment of these diseases is less clear than in AML or MDS (Figure 2c). The inconsistency of conditioning regimens, donor sources, GVHD prophylaxis and high degree of *in vivo* T-cell depletion all introduce additional variables and prevent reliable comparison of our study with controlled transplant trials of relapsed/refractory AML and high-risk MDS patients.[9,16] Interpretation of transplant outcomes is also limited by the fact that two patients did not proceed directly to HCT after clofarabine (due to lack of effective cytoreduction) and both achieved cytoreduction with alternative therapy before HCT. Nevertheless, this prospective trial confirms the feasibility and potential therapeutic benefit of the clofarabine cytoreduction approach by allowing the majority of high-risk MDS/AML patients to proceed to transplant with variable graft sources and conditioning regimens.

Although long-term outcomes remain poor, 6-month and 1-year OS (46%) and PFS (25%) rates compare favorably with previously published results for patients with active disease receiving HCT.[3,6,27] Many of these patients would not be widely recommended for transplant due to high-risk features beyond active disease: median age 51 years; 61% lacked a matched related donor; a majority with poor-risk cytogenetic features and circulating blasts at clofarabine initiation; 21% were intermediate and 24% high risk by the HCT-CI score; and the median relapsed/refractory AML pre-transplant risk score was 2 (n = 15, range 0–5) indicating an estimated 1 year OS of 25% for AML patients.[4]

Future trials in relapsed/refractory leukemia patients should consider primary endpoints such as cytoreduction or the likelihood of proceeding to transplant.[28,29] Alternative chemotherapeutics with non-overlapping toxicities to common transplant conditioning regimens must be validated for tolerable cytoreduction. Interestingly, the combination of ara-C and clofarabine led to higher rates of remission for relapsed/ refractory AML patients at the time of HCT as compared with ara-C alone, although the effectiveness at cytoreduction remains uncharacterized.[26,30]

The low 6-month relapse rate (28.6%), combined with the low NRM and minimal GVHD, indicates that this platform is a strong base from which to investigate post HCT maintenance interventions. Chronic GVHD is known to be associated with protection from relapse,[31] and the low incidence of cGVHD with the clofarabine bridge is likely associated with *in vivo* T depletion (alemtuzumab = 23, ATG = 5).[32] T-cell depletion remains controversial as enhanced tolerance and reduced GVHD comes at the expense of relapse without clearly

improving survival.[32,33] However, high disease risk also predisposes to higher NRM and our series affirms high-tolerance and low GVHD risks.

Building upon this platform should allow for development of GVL with permissible GVHD. DLI is associated with GVL and prolonged survival for patients relapsing after HCT,[34] although efficacy for AML/MDS is limited to patients having > 6 months remission duration after HCT.[35] A strategy of planned DLI may induce GVL for patients with minimal or undetectable disease.[36,37] An alternative, and possibly synergistic, strategy would be to initiate an immunomodulator, hypomethylating agent or molecularly targeted drug between 100 days and 6 months after HCT.[38–41]

In conclusion, this novel bridge approach allows for a short interval from salvage to transplant (median 21 days from clofarabine initiation to transplant), minimizes progression or failure to respond as ineligibility criteria for transplant (27/29 patients proceeded to conditioning at the nadir after 1 cycle of clofarabine), and avoids attrition of transplant eligible patients due to toxicity and morbidity associated with repeated induction therapy (1 patient died in remission before day 100 after transplant). Clofarabine cytoreduction immediately before allograft conditioning is well tolerated and permits high-risk patients to proceed to transplant with low NRM, making it an ideal platform for testing post-transplant maintenance strategies.

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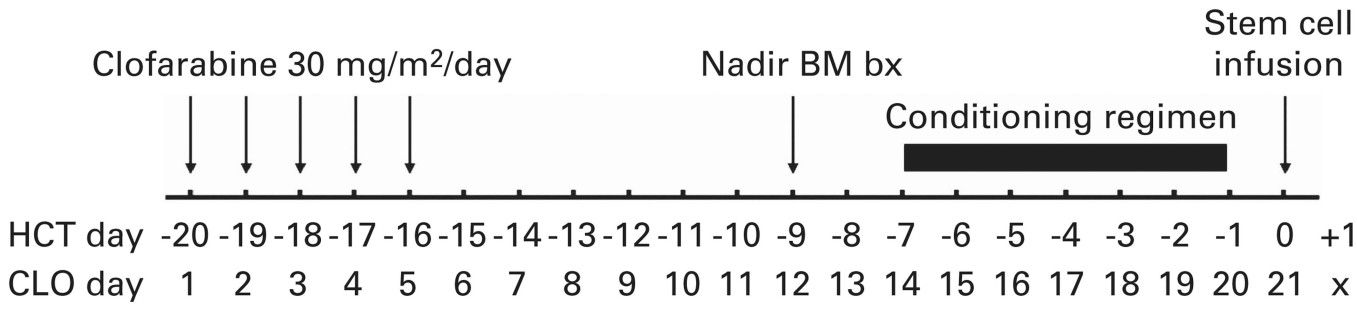

Figure 1.

Treatment schema and estimated chronology. Relative days are presented in relationship to both clofarabine and transplant. Before therapy, donor arrangements were made and patients were scheduled to begin conditioning between 12 and 21 days from the first day of clofarabine initiation. Nadir BM biopsy was done 12 days after clofarabine initiation.

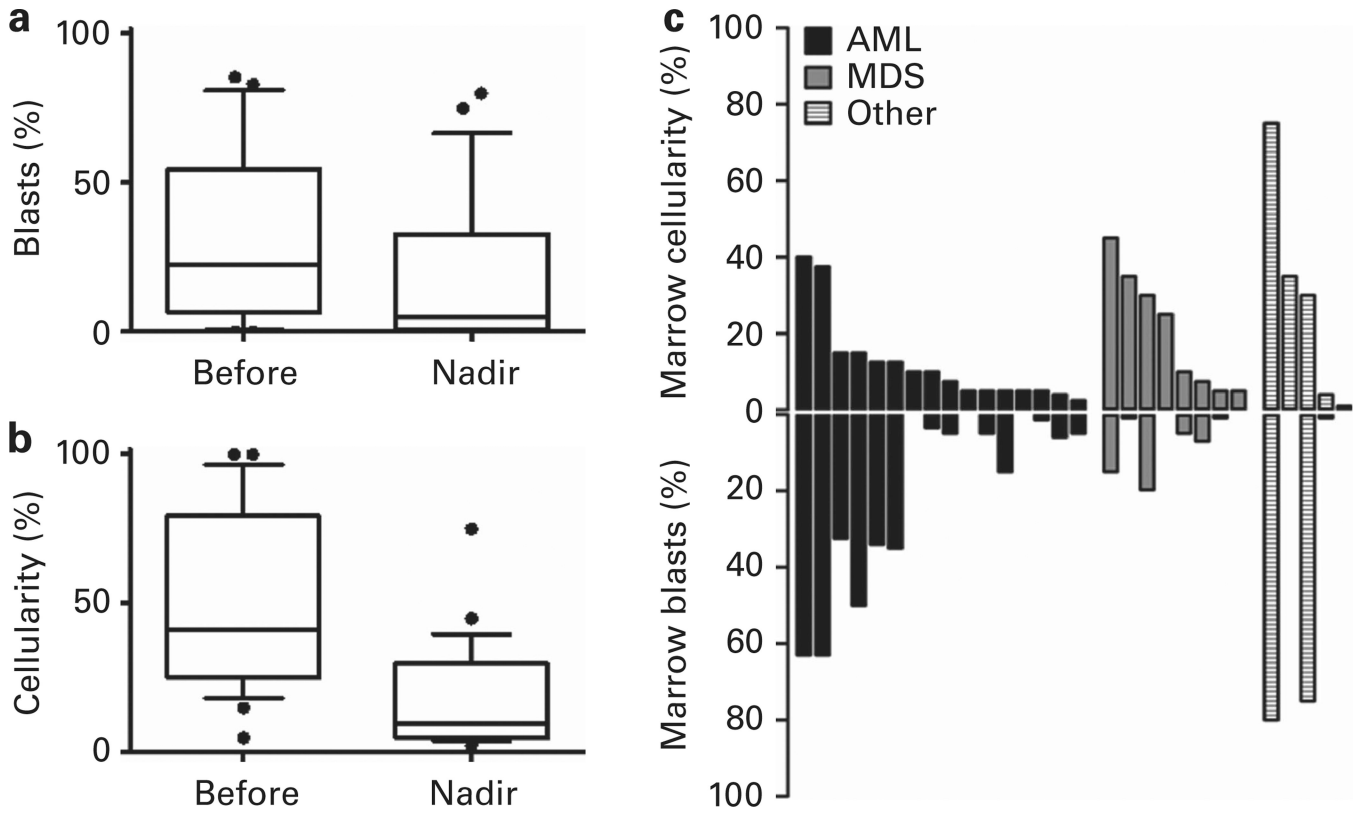

Figure 2.

BM disease burden. BM disease burden is reduced after clofarabine. (**a**) The median BM blast percentage was 22% (mean = 30%, range 0–86%) before clofarabine and 5% (mean = 18%, range 0–75%) after clofarabine ($P = 0.035$). (**b**) The median BM cellularity was 41% (mean = 31%, range 5–100%) before clofarabine and 10% (mean = 17%, range 1–75%) after clofarabine ($P < 0.0001$). (**c**) Post clofarabine nadir BM cellularity and blasts by disease category. Each column represents a single patient's result.

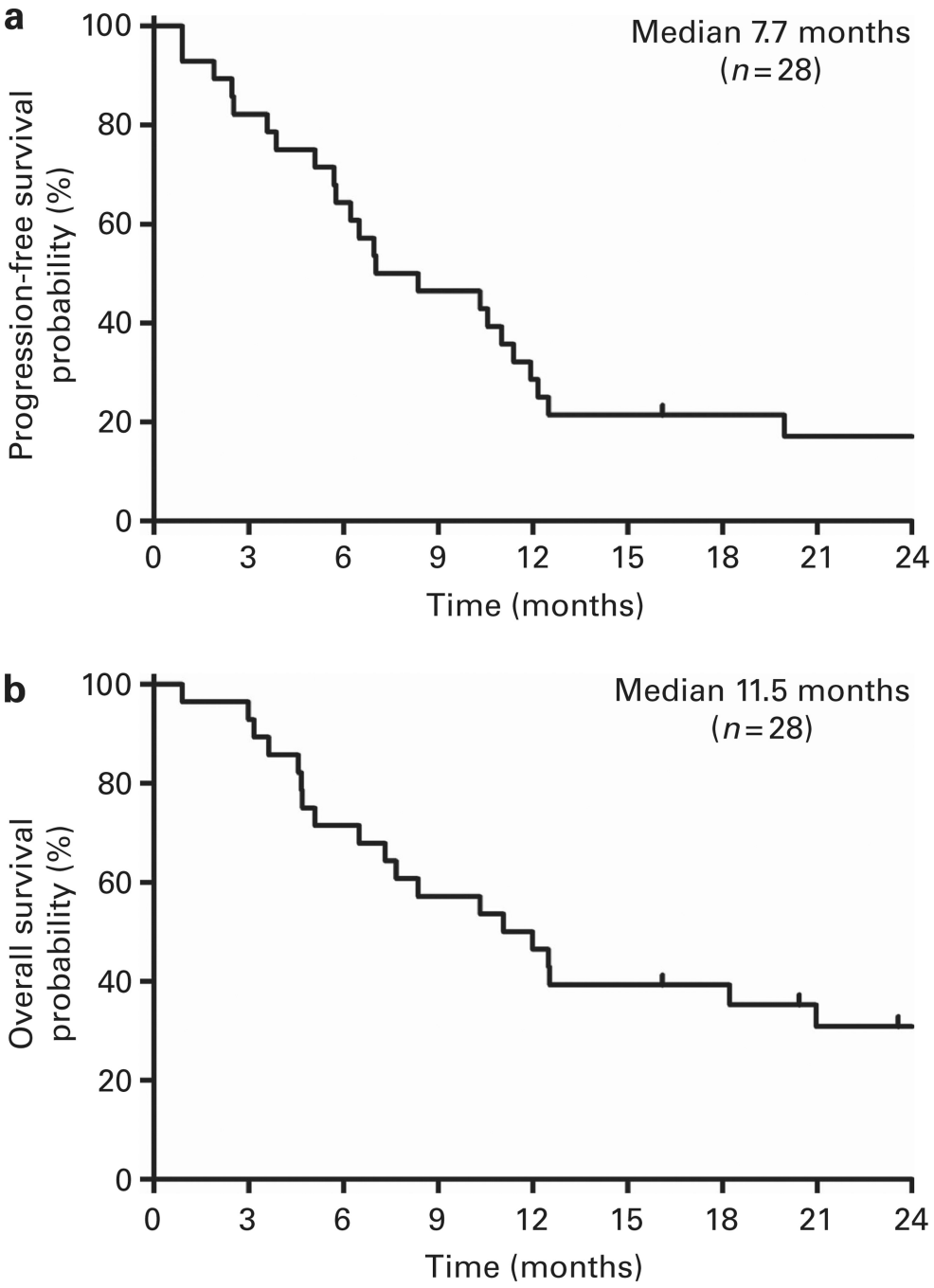

Figure 3.

Kaplan–Meier curves from the time of transplant. (**a**) Kaplan–Meier plot of PFS for transplanted patients and (**b**) OS for transplanted patients, in months from the time of transplant.

Table 1

Patient and transplant characteristics

Patient characteristics (*n* = 29)		**Transplant characteristics (*n* = 28)**	
Gender		*Patients proceeding to HCT*	*28*
Male	16	HCT within 30 days of clofarabine	26
Female	13	Days clofarabine to conditioning (median)	14
Median age, years	51	(range)	(11–68)
Range	(23–69)	Days clofarabine to HCT (median)	21
Disease/disease state		*(Range)*	*(17–75)*
ALL	2	Donor	
REL1	1	Matched related	11
REL2	1	Matched unrelated	12
MPD	3	Haploidentical + cord blood	5
MDS	8	Source	
Therapy related MDS	1	Peripheral blood	22
Prior response to hypomethylator	0	BM	1
AML	16	Cord blood	5
PIF	9	Conditioning regimen:	
REL1	6	CLofarabine/melphalan/alemtuzumab	3
REL2	1	Fludarabine/BU/ alemtuzumab	2
Refractory to last therapy	12	Fludarabine/melphalan/ alemtuzumab[a]	17
Therapy related AML	2	Fludarabine/melphalan/ ATG	5
Antecedent MDS	3	TBI/etoposide	1
Marrow blast%, median (*n* = 16)	40	TBI/etoposide/alemtuzumab	1
Range	(7.5–86)	GVHD prophylaxis	
Peripheral blood blast%, median (*n* = 16)	3.5	Tacrolimus/alemtuzumab[a]	23
Range	(0–81)	Tacrolimus/MMF/ATG	5
Cytogenetic risk group at diagnosis		*Tacrolimus/MMF*	*1*
Adverse	16	CMV serostatus	
Intermediate	12	Recipient and/or donor positive	18
Favorable	0	Recipient and donor negative	10
HCT-comorbidity index, range	*(0–5)*	*Donor gender (adult only)*	
Low (0)	16	Female	8
Intermediate (1–2)	6	Male	15
High (3 or more)	7	Median donor age (adult only)	41
Prior treatment		*(Range)*	*(21–72)*
None	2		
1 Prior regimen	10		
2 Prior regimens	9		
3 Or more prior regimens	8		

Abbreviations: CMV = cytomegalovirus; HCT = hematopoietic cell transplant; MDS = myelodysplastic syndrome; MPD = myeloproliferative disorder; PIF = primary induction failure; REL1 = first relapse; REL2 = second relapse. REL1, REL2, PIF, chronic phase (CP), accelerated phase

(AP), MPD, CML, conditioning regimens have all been previously reported and included: fludarabine 30 (FLU) mg/m^2/day i.v. on day − 7 through − 3 + melphalan (MEL) 140 mg/m^2 on day –2 + alemtuzumab (ALEM) (100mg total) on day − 7 through − 3; clofarabine (CLO) 30 mg/m^2/day i.v. on day − 7 through − 3 + MEL 140 mg/m^2 on day −2 + ALEM (100mg total) on day − 7 through − 3; FLU mg/m^2/day i.v. on day − 7 through − 3 + BU 3.2 mg/kg/day i.v. on day −6 through −3 (BU) + ALEM (100mg total) on day − 7 through − 3; TBI 1200 cGY + etoposide 60 mg/kg i.v. on day − 3 ± ALEM (100 mg total) on day − 7 through −3 for ALL patients; or FLU on day − 7 to − 3 + MEL 70 mg/m^2/day i.v. on day −3 to − 2 + rATG 1.5 mg/kg i.v. (6 mg/kg total) on day − 7, − 5, − 3, − 1 (flu/mel/ATG) for cord blood recipients. All cord blood units were supplemented with additional CD34-selected haplo-identical related adult peripheral blood stem cells.

[a] Includes patient that did not receive transplant.

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Table 2

Toxicities

Toxicity assessment[a] (*n* = 29)						
	Total toxicity (*n* = 29)		Clofarabine to conditioning (*n* = 29)		Conditioning to day + 12 (*n* = 29)	
	Grade 1–2	Grade 3–4	Grade 1–2	Grade 3–4	Grade 1–2	Grade 3–4
Renal (creatinine)	9 (31%)	1 (3%)	2 (7%)	0	9 (31%)	1 (3%)
Hepatic (total bilirubin)	14 (48%)	3 (10%)	12 (41%)	2 (7%)	8 (28%)	0
Hepatic (SGOT)	14 (48%)	9 (31%)	14 (48%)	7 (24%)	17 (59%)	3 (10%)
Cardiac	2 (7%)	0	0	0	2 (7%)	0
Skin	1 (3%)	0	1 (3%)	0	0	0
Infection	0	12 (41%)[b]	0	3 (10%)	0	10 (34%)[b]

[a] All toxicities calculated by CTCAE v.3 grading criteria expressed as % of patients experiencing the maximum toxicity level achieved during the indicated time period.

[b] Includes one grade 5 from sepsis on day − 1.

Table 3

Outcomes after transplant

Outcomes after allo-SCT				
	Entire cohort (*n* = 28)		AML/MDS (*n* = 23)	
	%	95% CI	%	95% CI
Relapse risk				
100 Days	14%	4–30	13%	3–30
6 Months	29%	13–46	26%	10–45
1 Year	54%	36–74	61%	36–78
Non-relapse mortality				
100 Days	4%	0–16	0%	
6 Months	7%	1–21	4%	0–19
1 Year	18%	6–34	13%	3–30
PFS				
100 Days	82%	62–92	87%	65–96
6 Months	64%	44–79	70%	47–84
1 Year	25%	11–42	26%	11–45
OS				
100 Days	89%	70–96	96%	79–99
6 Months	71%	51–85	78%	55–90
1 Year	46%	28–63	52%	31–70

Abbreviations: CI = confidence interval; MDS = myelodysplastic syndrome.