T-cell-replete haploidentical transplantation *versus* autologous stem cell transplantation in adult acute leukemia: a matched pair analysis

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ABSTRACT

Adult patients with acute leukemia in need of a transplant but without a genoidentical donor are usually considered upfront for transplantation with stem cells from any other allogeneic source, rather than autologous stem cell transplantation. We used data from the European Society for Blood and Marrow Transplantation and performed a matched pair analysis on 188 T-cell-replete haploidentical and 356 autologous transplants done from January 2007 to December 2012, using age, diagnosis, disease status, cytogenetics, and interval from diagnosis to transplant as matching factors. "Haploidentical expert" centers were defined as having reported more than five haploidentical transplants for acute leukemia (median value for the study period). The median follow-up was 28 months. Multivariate analyses, including type of transplant categorized into three classes ("haploidentical regular", "haploidentical expert" and autologous), conditioning intensity (reduced intensity *versus* myeloablative conditioning) and the random effect taking into account associations related to matching, showed that non-relapse mortality was higher following haploidentical transplants in expert (HR: 4.7; P=0.00004) and regular (HR: 8.98; $P<10^{-5}$) centers. Relapse incidence for haploidentical transplants was lower in expert centers (HR:0.39; P=0.0003) but in regular centers was similar to that for autologous transplants. Leukemia-free survival and overall survival rates were higher following autologous transplantation than haploidentical transplants in regular centers (HR: 1.63; P=0.008 and HR: 2.31; P=0.0002 respectively) but similar to those following haploidentical transplants in expert centers. We conclude that autologous stem cell transplantation should presently be considered as a possible alternative to haploidentical transplantation in regular centers that have not developed a specific expert program.

Introduction

Despite recent improvements in the prognosis and treatment of acute myeloid leukemia (AML) and acute lymphoid leukemia (ALL) in adults, disease relapse continues to affect most patients who are not transplanted.[1,2]

Transplant with cells from a genoidentical donor remains the gold standard treatment, but in the absence of a genoidentical sibling, patients are usually offered, as a second best choice, an allogeneic transplant using a matched unrelated donor or cord blood. Autologous stem cell transplantation (ASCT) has become less popular.[3]

Haploidentical stem cell transplantation has long remained associated with high non-relapse mortality despite some improvement brought by T-cell depletion and megadose CD34$^+$ stem cell infusion.[4-7] Initially considered as highly experimental and limited to a few specialized centers, haploidentical transplantation has recently emerged as a new and popular alternative transplant modality. It is now easier to perform than in the past, thanks to the shift from T-cell-depleted grafts to T-cell-replete marrow and/or peripheral blood stem cells.[8] In addition, an important reduction in toxicity has been observed with the introduction of high-dose cyclophosphamide after the transplantation, which has considerably reduced the incidence and severity of graft-*versus*-host disease (GVHD).[9-11]

ASCT has been used widely for consolidation chemotherapy in patients with acute leukemias, mostly AML in first (CR1) or second (CR2) complete remission over the past few decades.[12,13] ASCT remains a therapeutic option for AML because it has been consistently shown to be associated with a decreased relapse incidence and a better leukemia-free survival when compared to conventional chemotherapy. However, it is not associated with a graft-*versus*-leukemia effect, and the relapse incidence after ASCT is higher than after allogeneic transplantation.[12] Moreover, the development of reduced-intensity conditioning has made allogeneic transplantation feasible even in fit older patients up to 70–75 years of age, which has contributed to the decline of ASCT. However, allogeneic stem cell

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transplantation, although correlated with a lower relapse incidence, remains associated with a higher incidence of non-relapse mortality, GVHD, and infections. In addition, allogeneic transplant survivors tend to have a poorer quality of life than that of patients who undergo ASCT.[14]

As it stands, allogeneic stem cell transplantation with a genoidentical donor is associated with the best outcome but there has been no randomized or retrospective study showing the superiority of allogeneic transplantation using an alternative donor compared to ASCT in AML. Data in ALL are more limited.

In order to compare the outcome of adult patients following haploidentical and autologous transplants, we collected information available in the European Society for Blood and Marrow Transplantation (EBMT) registry, after January 2007 (when T-cell-replete haploidentical transplants were first reported) and conducted a matched pair analysis.

Methods

The study design was approved by the Acute Leukemia Working Party, in accordance with the EBMT guidelines for retrospective studies. In the period between January 2007 and December 2012, 2259 ASCT and 234 T-cell-replete haploidentical stem cell transplants were reported to the EBMT registry as first transplants to treat adult patients with either AML or ALL in CR1 or CR2.

For the matched pair analysis, we used as matching factors: age ± 5 years, diagnosis (AML, ALL), the status at transplant (CR1, CR2), the interval from diagnosis to transplant (CR1: less than or greater than 6 months; CR2: less than or greater than 18 months), and cytogenetic status. We identified 188 haploidentical transplants and 356 ASCT.

Endpoint definitions and statistical analysis

Four outcomes were evaluated: (i) non-relapse mortality, defined as death without previous relapse; (ii) relapse incidence, defined on the basis of morphological evidence of leukemia in bone marrow or other extramedullary organs; (iii) leukemia-free survival, defined as the time from transplantation to first event (either relapse or death in complete remission); and (iv) overall survival. Cumulative incidence curves were used for relapse incidence and non-relapse mortality in a competing risks setting, since death and relapse are competing.[15] Probabilities of overall survival and leukemia-free survival were calculated using the Kaplan–Meier estimate.[16] Within matched groups, associations were accounted for by a random effect common to both members from the same group using a Cox proportional hazards model.

All tests were two-sided with the type I error rate fixed at 0.05. Statistical analyses were performed with SPSS 19 (SPSS Inc., Chicago, IL, USA), and R 3.0.1 (R Development Core Team, Vienna, Austria) software packages.

Since haploidentical transplantation is a new, evolving transplant modality, we hypothesized the possibility of a center or a learning effect and compared the outcome of patients transplanted in "haplo expert" *versus* "regular" transplant centers defined according to the median number of haploidentical transplants for acute leukemia performed in the study period.

Table 1. Distribution of the matched pair populations of patients receiving a T- cell replete haploidentical transplant or an autograft.

		Autografts	Haploidentical	Global	*P* value
Number		356	188 (123 MAC; 65 RIC)		
Follow-up (months)		28(1–87)	27 (1–81)	28 (1–87)	0.93
Median age (years)		43 (18–71)	42 (18–69)	43 (18–71)	0.55
Age	>=50y	114 (32%)	63 (34%)	177 (33%)	0.73
Median year of transplant		2009 (07–12)	2011 (07–12)	2009 (07–12)	<0.0001
Interval diagnosis to transplant (days)	Global	207 (89–4172)	238 (82–3689)	214 (82–4172)	0.06
	CR1	194 (89–1060)	203 (82–879)	196 (82–1060)	0.20
	CR2	548 (123–4172)	555 (159–3689)	554 (123–4172)	0.61
Patients' gender	Male	199 (56%)	111 (59%)	310 (57%)	0.48
Diagnosis	AML	253 (71%)	132 (70%)	385 (71%)	
	ALL	103 (29%)	56 (30%)	159 (29%)	0.84
Status at transplant	CR1	283 (80%)	144 (77%)	427 (79%)	
	CR2	73 (21%)	44 (23%)	117 (22%)	0.43
Cytogenetics in AML	Good	21 (12%)	10 (13%)	31 (12%)	
	Intermediate	138 (79%)	60 (76%)	198 (78%)	
	Poor	15 (9%)	9 (11%)	24 (9%)	0.77
	NA/failed	79	53	132	
Cytogenetics in ALL	Ph negative	33 (47%)	20 (51%)	53(49%)	
	Ph positive	37 (53%)	19 (49%)	56 (51%)	0.68
	NA/failed	33	17	50	
Source of stem cells	BM	5%	50%	20%	
	PB	93%	47%	77%	
	BM+PB	2%	3%	2%	<0.0001
Total body irradiation	Yes	70 (20%)	55 (21 RIC) (29%)	125 (23%)	0.012
Engraftment	Engraftment	345 (98%)	176 (95%)	521 (97%)	0.03

ALL: acute lymphoid leukemia; AML: acute myeloid leukemia; BM: bone marrow; CR1: first complete remission; CR2: second complete remission; MAC: myeloablative conditioning; NA: not available; PB: peripheral blood; Ph: Philadelphia chromosome; RIC: reduced-intensity conditioning.

Results

Patients and centers

Table 1 shows the distribution of the two populations (haploidentical and autologous transplant recipients). Haploidentical transplants were more recent than ASCT (median year 2011 *versus* 2009; $P<10^{-4}$). The median follow up was 27 months (range 1-81) in the haploidentical group and 28 months (range 1-87) in the ASCT group.

For haploidentical transplants, 59 centers were classified as "regular" centers having done less than five haploidentical transplants during the study period [median 2 (range 1-5)] and nine as "expert" centers having done more than five [median number 12 (range 6-18)].

There was no difference in the two populations for cytogenetics classified as good, intermediate and poor risk for AML and Philadelphia chromosome (*BCR/ABL*)-negative or -positive for ALL. Interestingly in the ALL population, the proportion of Philadelphia-positive cases was high (51%).

The interval from diagnosis to transplant was 238 days (range, 82-3689) before haploidentical transplant and 207 days (range, 89-4172) in the ASCT group (P=0.06). The source of stem cells was different with 50% bone marrow for haploidentical transplants *versus* only 5% for ASCT ($P<10^{-4}$). The pre-transplant regimen was also different (Table 2): in the haploidentical transplant population; 123 patients (65%) received myeloablative conditioning which included total body irradiation in 34 and busulfan in 74. Sixty-five patients (35%) received reduced intensity conditioning which included total body irradiation in 21, and fludarabine in 41. Details of GVHD prophylaxis in the hap-

Table 2. Details of the pretransplant regimens and GVHD prophylaxis in haploidentical transplants.

HAPLO IDENTICAL

	MAC	RIC
Busulfan + cyclophosphamide	29	0
Busulfan + fludarabine	37	20
Fludarabine + melphalan	3	4
Threosulfan + cyclophosphamide	4	0
Threosulfan + fludarabine	6	10
Cyclophosphamide + fludarabine	8	7
Cyclophosphamide +thiotepa	2	0
Total body irradiation	34	21
Other	0	3

AUTOLOGOUS

Busulfan + cyclophosphamide	128
Busulfan + fludarabine	9
Busulfan ± other	40
Melphalan based	71
Cyclophosphamide +thiotepa	7
BEAM	16
Total body irradiation	70
Other	15

GVHD prophylaxis

	N
CSA+methotrexate	24
CSA+MMF	11
CSA+methotrexate+MMF	51
CSA+MMF+ cyclophosphamide	23
Tacrolimus+MMF+ cyclophosphamide	18
Sirolimus+MMF	18
Tacrolimus+MMF	14
Other	21
Unknown	8

BEAM: BCNU + etoposide + aracytine + high dose melphalan; CSA: cyclosporine A; MMF: mycofenolate mofetil.

Table 3. Results of autografts and T-cell-replete haploidentical transplants in the overall population, and in different subgroups.

	RI	NRM	LFS	OS
All patients				
Auto (n=356)	48% [42-53]	3% [2-6)	49% [43-55]	65% [59-70]
Haplo (n=188)	29% [22-37]	26% [21-33]	44% [36-52]	53% [45-60]
P	$<10^{-5}$	$<10^{-5}$	0.49	0.007
CR1 patients				
Auto (n=283)	46% [4--3]]	2% [1-4]	52% [45-59]	68% [62-75]
Haplo (n=144)	27% [19-35]	27% [19-36]	46% [37-55]	56% [47-64]
P	$<10^{-5}$	$<10^{-5}$	0.25	0.005
CR2 patients				
Auto (n=73)	54% [40-66]	1 % [4-19]	36% [24-48]	50% [37-63]
Haplo (n=44)	39% [23-55]	24% [14-35]	37% [21-53]	42% [26-59]
P	0.02	0.08	0.34	0.72
AML patients				
Auto (n=253)	50% [43-56]	4% [2-7]	47% [40-54]	64% [58-71]
Haplo (n=132)	27% [19-35]	25% [19-32]	48% [39-58]	57% [48-66]
P	$<10^{-5}$	$<10^{-5}$	0.73	0.12
AML CR1 intermediate cytogenetics				
Auto (n=116)	47% [36-56]	2% [0.3-0.6]	52% [42-62]	71% [62-80]
Haplo (n=50)	25% [14-38]	28% [17-41]	47% [33-61]	58% [44-71]
P	0.002	<10-5	0.78	0.03
ALL patients				
Auto (n=103)	44% [32-54]	3% [1-9]	54% [42-65]	66% [55-77]
Haplo (n=56)	36% [22-50]	30% [17-44]	34% [20-48]	40% [26-55]
P	0.13	<10-5	0.05	0.01
ALL CR1 Philadelphia negative				
Auto (n=26)	43% [20-63]	0	57% [35-79]	66% [46-88]
Haplo (n=14)	37% [12-63]	7% [0-18]	56% [29-82]	60% [32-88]
P	0.52	0.09	0.94	0.91
ALL CR1 Philadelphia positive				
Auto (n=36)	36% [19-53]	4% [0.3-18]	60% [42-78]	76% [61-92]
Haplo (n=17)	32% [11-55]	43% [21-63]	26% [4-47]	26% [4-47]
P	0.86	0.0006	0.005	0.001
Auto (n=356)	48% [42-54]	3% [2-6]	49% [43-55]	65% [59-70]
Haplo MAC (n=123)	26% [18-35]	27% [15-40]	47% [38-57]	55% [46-64]
Haplo RIC (n=65)	36% [23-49]	27% [15-40]	37% [24-51]	47% [33-61]
P	<10-5	<10-5	0.52	0.02
1. haplo ≤ 5 Tx (n=92)	35% [24-47]	34% [28-40]	31% [19-42]	42% [29-55]
2. haplo > 5 Tx (n=96)	25% [17-35]	20% [15-26]	54% [44-65]	60% [50-70]
3. autograft (n=356)	48% [42-54]	3% [2-6]	49% [43-55]	65% [59-70]
P global	10^{-5}	$<10^{-5}$	0.001	0.0003
P 1 *versus* 3	0.03	$<10^{-5}$	0.003	$<10^{-5}$
P 2 *versus* 3	$<10^{-5}$	$<10^{-5}$	0.16	0.48

ALL: acute lymphoid leukemia; AML: acute myeloid leukemia; Auto: autologous transplantation; Haplo: T-cell-replete haploidentical transplant; CR1: first complete remission; CR2: second complete remission; LFS: leukemia-free survival; MAC: myeloablative conditioning; Tx: transplant; NRM: non-relapse mortality; OS: overall survival; PH+: Philadelphia chromosome-positive; RI: relapse incidence; RIC: reduced intensity conditioning.

loidentical group are given in Table 2. The proportion of patients receiving cyclophosphamide after transplantation as a GVHD prophylaxis measure (available only in 50% of the patients) was 36% (41 patients). In the ASCT population, 70 patients received high-dose total body irradiation (20%), and 286 received chemotherapy-only combinations (80%) consisting of busulfan + cyclophosphamide in 126, and busulfan with another combination in 49. Successful engraftment occurred in 95% of the haploidentical transplants and 98% of the ASCT (P=0.03). In all, 78/188 patients in the haploidentical transplant group died, mainly from transplant toxicity (n=50) and relapse (n=28), while 119/356 patients in the ASCT group died, mainly from relapse (n=89). Fifty-four autografted patients and eight haploidentical transplant recipients subsequently had another allogeneic transplant after relapse.

Outcome

Table 3 provides the results by univariate analysis in the overall population and in different subgroups.

In the overall population, the non-relapse mortality rate was significantly higher following haploidentical transplants (26% *versus* 3%; $P<10^{-5}$), while the relapse incidence was significantly higher following ASCT (48% *versus* 29%, $P<10^{-5}$). Leukemia-free survival was not significantly different (Figure 1A,C). The overall survival was significantly higher following ASCT (65% *versus* 53%; P=0.007). It was significantly higher in patients autografted in CR1 (68% *versus* 56%; P=0.005) (Figure 1B) but not in patients transplanted in CR2 (Figure 1D).

Regarding AML, there was no significant difference for leukemia-free survival and overall survival in the whole population. In AML, the overall survival in the intermediate cytogenetic risk group transplanted in CR1 (the biggest and most homogeneous group), was superior after ASCT (71% *versus* 58%; P=0.03).

Regarding ALL, leukemia-free survival and overall survival rates were better after ASCT in the overall population and in the Philadelphia-positive group: in the overall population the leukemia-free survival rate was 54% *versus* 34% (P=0.05) and overall survival 66% *versus* 40% (P=0.01). In the Philadelphia/BCR-ABL-positive group (36 autografts and 17 haploidentical transplants), ASCT in CR1 was associated with better non-relapse mortality (4% *versus* 43%;

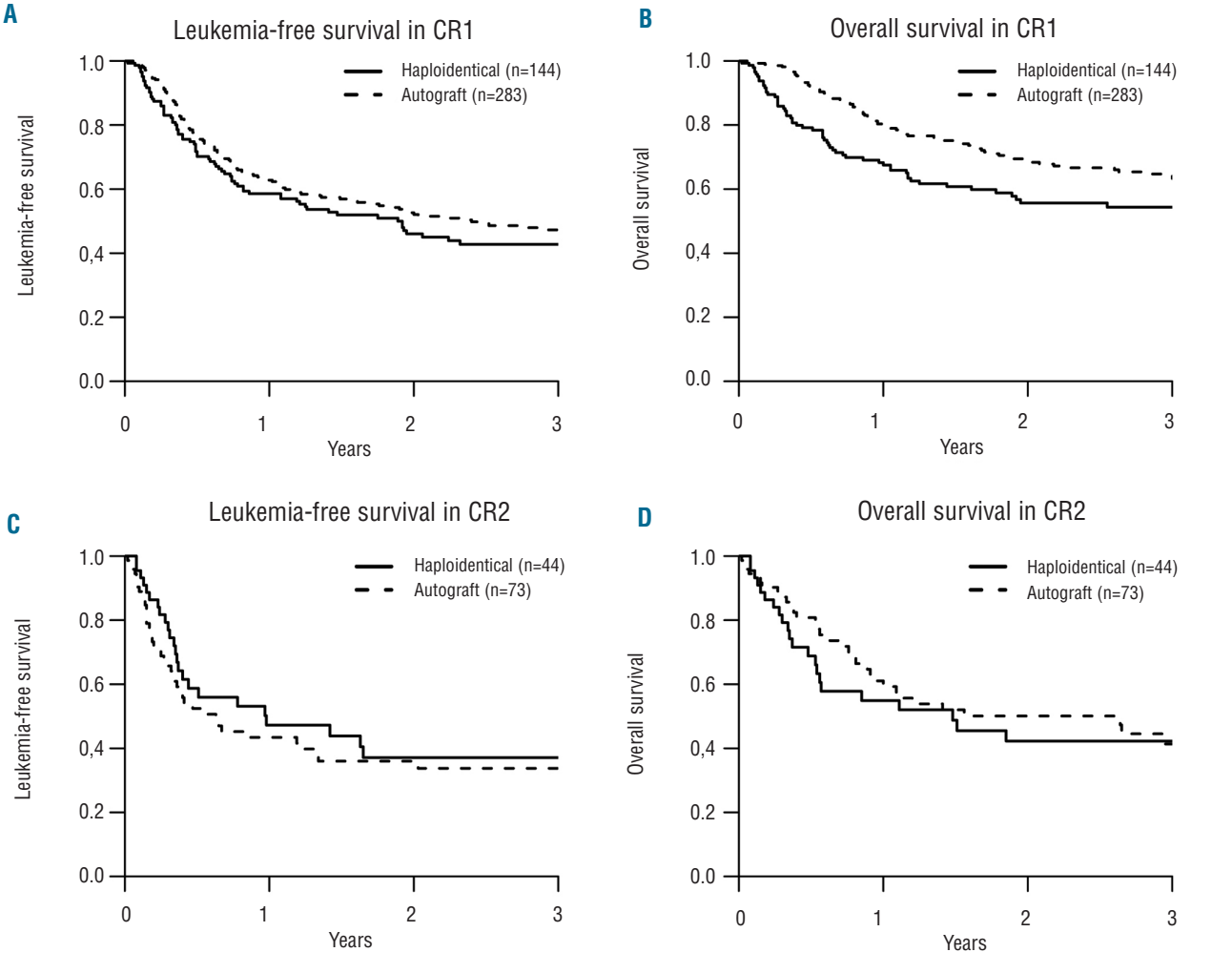

Figure 1. Leukemia-free survival and overall survival in patients transplanted in first (A, B) and second remission (C, D). Overall survival in patients transplanted in CR1 (B) is significantly higher following autologous stem cell transplantation (P=0.006).

P=0.0006), leukemia-free survival (60% *versus* 26%; *P*=0.005), and overall survival (76% *versus* 26%; *P*=0.001), while relapse incidence was not different (36% *versus* 32%; *P*=0.86). The two transplant modalities induced a similar outcome for ALL Philadelphia-negative patients transplanted in CR1.

When comparing ASCT (n=356) to haploidentical transplants with myeloablative conditioning (n=123) or reduced intensity conditioning (n=65), the relapse incidences were 48%, 26% and 36%, respectively ($P<10^{-5}$) and the overall survival rates were 65%, 55% and 47% (*P*=0.02).

Following relapse, 62 patients (54 after ASCT and 8 after haploidentical transplants) received a second (allogeneic) transplant: in the 54 patients initially autografted, the non-relapse mortality was 27%, the relapse incidence 40%, the leukemia-free survival 33% and the overall survival 41% at 2 years after the second transplant. Of the eight patients initially allografted, only one remains alive and well 2 years after the second allograft.

Patients who received an haploidentical transplant in haplo "expert" centers did better than those transplanted in "regular" centers (Figure 2). The overall survival rates were 65% for ASCT, 60% for haploidentical transplants in expert centers, and 42% for haploidentical transplants in regular centers.

Multivariate analyses

Results of multivariate analyses including type of transplant categorized into three classes (haplo regular, haplo expert and ASCT), conditioning intensity (reduced intensity versus myeloablative) and the random effect taking into account associations related to matching are summarized in Table 4.

Haploidentical transplants in "regular" centers were associated with significantly lower leukemia-free (Figure 2A) and overall (Figure 2B) survival rates than those following ASCT (HR:1.63, *P*=0.008 and HR: 2.31, *P*=0.0002, respectively). Leukemia-free and overall survival rates following haploidentical transplants in "expert" centers did not differ from those following ASCT, whereas the haploidentical transplants in the "expert" centers were associated with a lower relapse incidence than ASCT (HR: 0.39, *P*=0.0003).

Discussion

Following induction of complete remission, relapse remains a major issue in the therapeutic strategy for acute leukemia in adult patients. With some exceptions for "good risk" patients, the majority of teams tend to recommend hematopoietic stem cell transplantation to most patients in first or second remission.

In the absence of HLA identical siblings, HLA haploidentical parents and other family members have long been considered as alternative donors[17] since they are immediately available and involve less expense. Early attempts resulted in an unacceptable non-relapse mortality due to GVHD and infections. Later, the introduction of T-cell-depleted grafts and the use of megadoses of $CD34^+$ stem cells showed the feasibility of the approach; however, the technique has

Table 4. Multivariate analyses.

		HR	95% CI	*P*
OS	Type of transplant (global *P*)			0.0004
	Haplo (regular) *vs.* auto	2.31	1.50-3.58	0.0002
	Haplo (expert) *vs.* auto	1.16	0.76-1.76	0.50
	RIC *vs.* MAC	0.91	0.55-1.51	0.73
LFS	Type of transplant (global *P*)			0.04
	Haplo (regular) *vs.* auto	1.63	1.14-2.35	0.008
	Haplo (expert) *vs.* auto	0.75	0.51-1.09	0.13
	RIC *vs.* MAC	1.14	0.74-1.75	0.56
RI	Type of transplant (global *P*)			0.13
	Haplo (regular) *vs.* auto	0.87	0.53-1.44	0.59
	Haplo (expert) *vs.* auto	0.39	0.23-0.65	0.0003
	RIC *vs.* MAC	1.24	0.67-2.28	0.49
NRM	Type of transplant (global *P*)			$5x10^{-10}$
	Haplo (regular) *vs.* auto	8.98	4.41-18.29	$<10^{-5}$
	Haplo (expert) *vs.* auto	4.70	2.26-9.77	0.00004
	RIC *vs.* MAC	0.98	0.52-1.82	0.94

Regular center for haploidentical transplants: defined as reporting fewer transplants than the median value per center (n= 5/year). Expert centers for haploidentical transplants: defined as reporting more transplants than the median value per center (n= 5/year); haplo,T-cell-replete haploidentical transplant; LFS: leukemia-free survival; NRM: non-relapse mortality; OS: overall survival; RI: relapse incidence; HR: hazard ratio; CI: confidence interval.

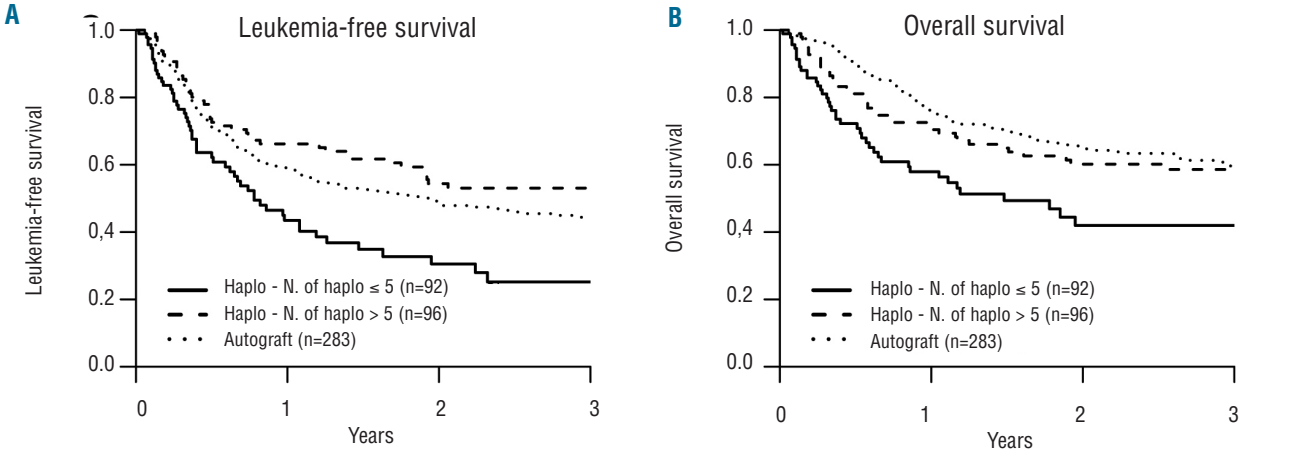

Figure 2. (A) Leukemia-free survival and (B) overall survival of patients autografted and patients receiving a haploidentical transplant in "haplo expert" *versus* regular transplant centers.

remained cumbersome and expensive, and therefore limited to a few pioneering centers.[4,5,18] Recently, the introduction of high-dose cyclophosphamide, to prevent GVHD,[9-11] has completely changed the field; thus, haploidentical transplantation is becoming an important area of investigation.[19-21] If successful, it may result in major advances in the choice of alternative donors, since almost all patients have such a donor.

Regarding ASCT, retrospective studies from various centers,[22-25] the EBMT[26,27] and the Center for International Blood and Marrow Transplantation Research (CIBMTR)[28] as well as numerous randomized studies[29-34] have indicated that the long-term leukemia-free survival of AML patients autografted in CR1 is approximately 50%, whereas that for patients autografted in CR2 is approximately 30%. Results in ALL have been inferior. ASCT has become less popular mainly because it is associated with a high incidence of relapses, including late relapses (data submitted for publication).[35] Although a recent retrospective study from the CIBMTR[28] concluded that, in the absence of a matched sibling donor, ASCT may provide an acceptable alternative post-remission therapy for patients with AML in CR1, it is generally proposed as a last option. We, therefore, considered it important to compare outcomes of ASCT and haploidentical transplants in the EBMT registry. To do this, we selected recent haploidentical transplants defined as T-cell-replete, which were first reported in 2007, and did a matched pair analysis, using as matching factors the five characteristics we found most pertinent and which were available in the registry. Fifty percent of haploidentical transplants reported to the EBMT registry were from centers that had developed a haplotransplant program and had performed more than five haploidentical transplants for acute leukemia. We, therefore, found it important to compare the outcome of transplants performed in these centers and in centers with less experience.

What this study shows is that the outcome of patients autografted was similar (and not inferior) to the outcome of patients who received a haploidentical transplant when performed in expert centers but not in regular centers. In regular centers, leukemia-free survival and overall survival rates were superior after ASCT. This finding indicates that a center effect study in the field of haploidentical transplants should be carried out as has been done for genoidentical transplants and, more recently, for reduced intensity conditioning transplants.[36] The population of haploidentical transplanted patients was heterogeneous regarding conditioning with myeloablative conditioning or reduced intensity conditioning. Our study was not designed to compare these various modalities although preliminary data suggest that the relapse incidence following reduced intensity conditioning is higher than that following myeloablative conditioning.[37]

As expected, this study confirms the higher relapse incidence following ASCT and the higher non-relapse mortality after haploidentical transplantation. We paid particular attention to the group of patients with intermediate cytogenetic risk AML because it was the biggest and most homogeneous group and still represents the gray zone for transplantation guidelines: in this group, the overall survival was superior after ASCT. In ALL patients, those positive for the Philadelphia/*BCR-ABL* chromosome not only had a better overall survival but also a better leukemia-free survival following ASCT. The number of patients was, however, small and confirmation is needed in larger populations. Nonetheless, it is interesting that these observations are in accordance with the latest EBMT survey of the outcome of adult ALL patients autografted in the tyrosine kinase inhibitor era.[38]

When interpreting these data, there are at least three strong reservations: the first one is that 54 patients who relapsed after ASCT received a second allogeneic transplant and some were rescued with a leukemia-free survival and overall survival of 33% and 41%, respectively, which obviously contributed to the better results observed in the ASCT group. A second one is that the quality of life of survivors was not assessed while it was likely to be better after ASCT. The third reservation is that haploidentical T-cell-replete transplantation is a new and developing modality that is already showing improvement with time.

While these data are preliminary, they do indicate that in patients without an available HLA identical donor, considered for a transplant in CR1, ASCT should remain a possible alternative to haploidentical transplantation, at least in regular centers that have not developed a specific expert program. This proposal draws further support from the fact that, following relapse after ASCT, some patients can be rescued with allogeneic transplantation.

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Authorship and Disclosures

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