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Impact of Donor Type and Melphalan Dose on Allogeneic Transplantation Outcomes for Patients with Lymphoma

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A B S T R A C T

We analyzed 186 patients with lymphoma who underwent allogeneic stem cell transplantation (ASCT) with fludarabine-melphalan (FM) conditioning and different types of donors (25 haploidentical [HD], 98 matched unrelated [MUD], and 63 matched related [MRD]) at our institution between September 2009 and January 2018. Patients received fludarabine 160 mg/m^2 (40 mg/m^2/day for 4 days) in combination with 1 dose of melphalan 140 mg/m^2 (FM140) or 100 mg/m^2 (FM100). Engraftment was similar among the 3 groups (92%, 89%, and 98%, respectively; P = .7). The 6-month cumulative incidence of grade III-IV acute graft-versus-host disease (GVHD) was 4% in the HD group, 14% in the MUD group, and 8% in the MRD group (P not significant), and the respective 3-year cumulative incidence of chronic GVHD was 5%, 16%, and 26% (P not significant). The respective 3-year nonrelapse mortality and relapse rates were 31%, 32%, and 10% (HD versus MUD, P = .9; HD versus MRD, P = .02) and 15%, 21%, and 39% (HD versus MUD, P = .4; HD versus MRD, P = .04). At 3 years, progression-free survival (PFS) was 59%, 44%, and 46% (P not significant); overall survival (OS) was 52%, 54%, and 67% (P not significant); and GVHD-free, relapse-free survival was 39%, 31%, and 24% (P not significant). No differences in the 3-year PFS (57% versus 43%; P = .3) and OS (64% versus 58%; P = .7) were seen between patients receiving FM100 and those receiving FM140. Our data demonstrate that in patients with lymphoma, ASCT with HD transplants have similar outcomes as ASCT with HLA-matched transplants, and the FM100 conditioning regimen appears to be at least as effective as the FM140 regimen.

INTRODUCTION

Despite the recent advances in the treatment of patients with lymphoma, especially B cell non-Hodgkin lymphoma (NHL), many patients relapse and have poor outcomes [1-3]. Allogeneic stem cell transplantation (ASCT) is a potentially curative strategy for these patients, due at least in part to a potent graft-versus-lymphoma effect [4,5]. Most patients with lymphoma are heavily pretreated with multiple lines of chemotherapy before ASCT, and application of myeloablative conditioning regimens is usually associated with prohibitive nonrelapse mortality (NRM) [4]. Over the last decade, improved outcomes with the use of reduced-intensity conditioning (RIC)/nonmyeloablative (NMA) conditioning and haploidentical donor (HD)-ASCT performed with post-transplantation cyclophosphamide (PTCy)-based graft-versus-host disease (GVHD) prophylaxis [6] has renewed interest in this form of treatment, especially for patients with advanced Hodgkin lymphoma (HL), who were found to have remarkably good results with transplantation [7,8], whereas patients with NHL are increasingly considered for ASCT [9-11]. These strategies have extended safer transplantation to virtually all candidates, including non-Caucasians, because most patients will have a child, parent, or sibling as a potential donor for ASCT [12,13]. Recent studies comparing HD-ASCT with ASCT with a matched unrelated donor (MUD) and ASCT with a matched related donor (MRD) to treat lymphoma have shown similar outcomes [8,9,14-17]. However, most of these retrospective studies have included multiple transplantation conditioning regimens, confounding the interpretation of results. Fludarabine in

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combination with melphalan 140 mg/m^2 (FM140) has been used as a standard of care conditioning regimen for patients with lymphoma undergoing ASCT with an HLA-matched donor [18]. More recently, a modified version of this regimen—fludarabine and melphalan 140 mg/m^2 (FM140)—for HD-ASCT has been developed by our group [19].

Here we aimed to assess the impact of donor type and melphalan dose on outcomes of ASCT for patients who received FM-based conditioning at our institution.

METHODS

Study Design and Patients

In this retrospective study, we evaluated all consecutively treated patients with a diagnosis of lymphoma or chronic lymphocytic leukemia who underwent their first ASCT with an FM-based conditioning regimen between September 2009 and January 2018 at the University of Texas M.D. Anderson Cancer Center. Donor preference was MRD, followed by 10/10 MUD, and then HD. An HD was used when no MUD was available or when the transplantation was urgently needed. All patients provided written informed consent for transplantation according to the Declaration of Helsinki. The patients were treated on a clinical trial or according to the current institutional standard of care. The University of Texas M.D. Anderson Cancer Center's Institutional Review Board approved this retrospective study.

Conditioning Regimen and Transplantation

Patients received fludarabine 160 mg/m^2 administered i.v. in 4 daily doses (40 mg/m^2/day) in combination with melphalan 140 mg/m^2 (FM140) or 100 mg/m^2 (FM100). For the purpose of this study, patients receiving FM140 were considered to have received myeloablative conditioning (MAC), and those who received FM100 were considered to have received NMA conditioning. The FM100 regimen was used primarily in older patients or patients with significant comorbidities, because of concerns for toxicity. Thiotepa at a dose of 5 mg/kg or 2 Gy total body irradiation (TBI) was added for patients undergoing HD-ASCT to facilitate engraftment. In addition, patients with CD20$^+$ disease received rituximab 375 mg/m^2 on days −13, −6, +1, and +8 [20]. Most HD-ASCT recipients received a bone marrow (BM) graft, whereas MRD and MUD recipients received predominantly peripheral blood stem cells (PBSC) grafts. Standard infectious prophylaxis was provided to all transplant recipients with pentamidine or Bactrim, voriconazole, posaconazole or fluconazole, and acyclovir or valgancyclovir, as described previously [21].

GVHD Prophylaxis

Patients who underwent ASCT with an MRD or MUD received mini-methotrexate and tacrolimus. In addition, all MUD transplant recipients received antithymocyte globulin (ATG) for a total dose of 5 mg/kg. HD-ASCT recipients received PTCy 50 mg/kg on days +3 and +4, followed by mycophenolate mofetil (MMF) and tacrolimus starting on day +5 and continuing until 3 months and 6 months post-transplantation, respectively, followed by a weekly taper. The target tacrolimus level was 8 ng/mL (therapeutic level between 5 and 15 ng/mL), which was maintained for at least 6 months post-after transplantation and tapered weekly thereafter in the absence of signs and symptoms of GVHD. All patients received granulocyte-colony stimulating factor (G-CSF) starting on day +6 and continuing until engraftment.

Outcome Endpoints and Definitions

The primary outcome was progression-free survival (PFS), and secondary outcomes included engraftment rate, relapse, NRM, incidences of acute GVHD (aGVHD) and chronic GVHD (cGVHD), overall survival (OS), and GVHD-free, relapse-free survival (GRFS). Engraftment was defined as achievement of an absolute neutrophil count $\geq .5 \times 10^9$/L for 3 consecutive days before day +28 post-transplantation. Platelet recovery was defined as achievement of a platelet count $\geq$20,000/μL unsupported by platelet transfusions for 7 days. NRM events were defined as death without evidence of persistence or relapse of disease. OS was estimated from the time of transplantation to the date of last follow-up. GRFS was estimated as the time from transplantation to disease relapse, the onset of severe aGVHD and/or extensive cGVHD, or death from any cause. Toxicities were graded according to the National Institutes of Health Common Terminology Criteria for Adverse Events, version 5.

Statistical Analysis

Actuarial OS, PFS, and GRFS were estimated using the Kaplan-Meier method. The cumulative incidences of GVHD, NRM, and disease progression were estimated accounting for competing risks. Competing risks included disease progression and death from any cause for GVHD, death from persistent disease and disease progression for NRM, and death from persistent disease and NRM for disease progression. Predictors of OS, PFS, and GRFS were evaluated using Cox proportional hazards regression in univariate analysis and multivariate analysis (MVA) when indicated. Fine and Gray regression analysis was used to evaluate predictors of GVHD, NRM, and disease progression on univariate analysis and MVA. Characteristics were compared using the chi-square test for categorical variables and the Wilcoxon rank-sum test for continuous variables. Statistical significance was defined as $P < .05$. Statistical analyses were mainly performed using Stata 14.0 (StataCorp, College Station, TX).

RESULTS

Patient Characteristics

A total of 186 ASCT recipients were analyzed, including 25 with an HD, 98 with an MUD, and 63 with an MRD. Table 1 presents patient- and transplantation-related characteristics. The number of ASCTs performed according to histological subtypes were as follows: NHL (n = 93), HL (n = 58), and chronic lymphocytic leukemia/small lymphocytic lymphoma (n = 35). The histology for patients with NHL was diffuse large B cell lymphoma (n = 23), mycosis fungoides/Sézary syndrome (n = 20), follicular lymphoma (n = 7), composite/discordant lymphoma (n = 7), mantle cell lymphoma (n = 6), large cell anaplastic lymphoma (n = 4), hepatosplenic gamma-delta lymphoma (n = 3), extranodal marginal zone lymphoma (n = 1), and other rare histologies (n = 22).

There were no significant differences in characteristics among the 3 donor groups in terms of age, International Prognostic Index score, comorbidities, disease status at the time of ASCT, number of previous lines of chemotherapy, and response to salvage chemotherapy regimens, except that a higher proportion of patients in the HD group received an NMA regimen (64%, compared with 11% for MUD and 10% for MRD), and a BM graft (84%, compared with 35% for MUD and 2% for MRD). More patients in the HD group had advanced disease (stage III-IV) on initial presentation (77%, compared with 66% for MUD and 51% for MRD) (Table 1). However, there was no statistically significant difference in the Disease Risk Index distribution among the 3 groups ($P = .5$; Table 2).

Hematopoietic Recovery

The proportion of neutrophil engraftment was similar in the HD (reference), MUD, and MRD groups: 92%, 89% ($P = .7$), and 98% ($P = .3$), respectively. The respective median time to neutrophil recovery was 18 days, 12 days ($P < .001$), and 12 days ($P < .001$) days, and the respective median time to platelet recovery was 26 days, 14 days ($P < .001$), and 12 days ($P < .001$) days. The median peripheral blood T cell and myeloid chimerism was 100% donor on days +30 and +90 for all 3 donor groups.

aGVHD and cGVHD

The cumulative incidence of grade II-IV aGVHD at 6 months post-transplantation was 29% (95% confidence interval [CI], 16% to 55%; reference) in the HD group, 36% (95% CI, 28% to 47%; $P = .4$) in the MUD group, and 35% (95% CI, 25% to 49%; $P = .5$) in the MRD group, whereas the corresponding incidence of grade III-IV aGVHD at 6 months was 4% (95% CI, 1% to 28%; reference) in the HD group, 14% (95% CI, 8% to 23%; $P = .2$) in the MUD group, and 8% (95% CI, 3% to 18%; $P = .5$) in the MRD group. The incidence of cGVHD at 3 years was 5% (95% CI, 1% to 36%; reference) in the HD group, 16% (95% CI, 10% to 26%; $P = .2$) in the MUD group, and 26% (95% CI, 17% to 40%; $P = .09$) in the MRD group.

Relapse and NRM

In univariable analysis, the rate of disease relapse at 3 years was 15% (95% CI, 5% to 42%) in the HD group, 21% (95% CI, 14% to 31%) in the MUD group, and 39% (95% CI, 29% to 54%) in the MRD group (HD versus MUD, $P = .4$; HD versus MRD, $P = .04$)

Table 1
Patient Characteristics

Characteristic	HD Group (N = 25)	MUD Group (N = 98)	MRD Group (N = 63)	*P* Value, HD vs MUD	*P* Value, HD vs MRD
Age at ASCT, yr, median (range)	50 (20-65)	47 (20-71)	50 (18-72)	.5	.5
HCT-CI score, median (range)	1 (0-7)	2 (0-9)	2 (0-7)	.7	.3
HCT-CI score >3, n (%)	5 (20)	20 (20)	14 (22)	.6	.5
Diagnosis, n (%)					
CLL	5 (20)	17 (17)	13 (21)		
HL	4 (16)	33 (34)	21 (33)		
NHL	16 (64)	48 (49)	29 (46)	.2	.2
Disease stage at diagnosis, n (%)					
0	0 (0)	1 (1)	1 (2)		
1	1 (4)	6 (6)	13 (21)		
2	4 (16)	23 (23)	14 (22)		
3	4 (16)	13 (13)	9 (14)		
4	13 (52)	46 (47)	20 (32)		
Unknown	2 (8)	9 (9)	6 (10)		
3-4	17 (77)	59 (66)	29 (51)	.3	**.03**
Disease status, n (%)					
Active	18 (72)	76 (78)	44 (70)		
Remission	7 (28)	22 (22)	19 (30)	.6	.8
Previous response, n (%)					
Complete remission	9 (36)	36 (37)	28 (44)		
Partial remission	9 (36)	36 (37)	18 (29)		
Stable disease	5 (20)	17 (17)	14 (22)		
Progressive disease	2 (8)	9 (9)	3 (5)		
Complete/partial remission	7 (72)	72 (73)	46 (73)	.9	.9
Melphalan dose, n (%)					
100 mg/m^2	16 (64)	11 (11)	6 (10)	<.001	<.001
140 mg/m^2	9 (36)	87 (89)	57 (90)		
Cell source, n (%)					
Peripheral blood	4 (16)	63 (64)	62 (98)		
BM	21 (84)	35 (36)	1 (2)	<.001	<.001
Previous lines of chemotherapy, median (range)	3 (1-8)	3 (0-9)	3 (0-13)		
>4 previous lines of chemotherapy, n (%)	7 (28)	21 (21)	13 (21)	.5	.5
Treatment, n (%)					
Standard of care	14 (56)	58 (59)	40 (63)		
Protocol	11 (44)	40 (41)	23 (37)	.8	.5
IPI for lymphoma, n (%)					
0	7 (44)	22 (46)	10 (34)		
1	3 (19)	13 (27)	6 (21)		
2	3 (19)	4 (8)	5 (17)		
3	1 (6)	1 (2)	3 (10)		
Unknown	2 (13)	8 (17)	5 (17)		
>1	4 (29)	5 (13)	8 (33)	.1	.8

CLL indicates chronic lymphocytic leukemia; HCT-CI, hematopoietic cell transplantation comorbidity index; IPI, International Prognostic Index

(Table 3; Supplementary Table 1). MVA was not indicated for disease progression, because donor type was the sole significant predictor of the rate of progression. Compared with the HD group, the rate of disease progression was comparable in the MUD group (hazard ratio [HR], 1.6; *P* = .4) but significantly higher in the MRD group (HR, 3.4; *P* = .04).

In univariable analysis, the rate of NRM at 3 years was 31% (95% CI, 16% to 58%) in the HD group, 32% (95% CI, 24% to 43%) in the MUD group, and 10% (95% CI, 4% to 20%) in the MRD group (HD versus MUD, *P* = .9; HD versus MRD, *P* = .02) (Table 3; Supplementary Table 1). In MVA, compared with HD, NRM was significantly lower in the MRD group (HR, 0.3; 95% CI, .1 to .8; *P* = .02), but no different in the MUD group (HR, 1.1; 95% CI, .5 to 2.4; *P* = .8). Age >50 years was the only other significant variable associated with higher NRM (HR, 1.9; 95% CI, 1.1 to 3.5; *P* = .03) on MVA.

Survival

The median duration of follow-up among all surviving patients was 57 months (range, 3 to 101 months), including 34 months (range, 3 to 74 months) in the HD group, 62 months (range, 3 to 100 months) in the MUD group, and 54 months (range, 6 to 101 months) in the MRD group. At last follow-up, 107 patients (57%) were still alive. On univariable analysis, PFS at 3 years was 49% (95% CI, 26% to 69%) in the HD group, 44% (95% CI, 34% to 54%) in the MUD group, and 46% (95% CI, 33% to

Table 2
Patient Disease Index Risk Categories by Donor Type

Donor Type	Disease Index Risk Category			Total
	High	Intermediate	Low	
HD, n (%)	6 (24.0)	8 (32.0)	11 (44.0)	25 (100)
MUD, n (%)	11 (11.22)	34 (34.69)	53 (54.08)	98 (100)
MRD, n (%)	8 (12.70)	25 (39.68)	30 (47.62)	63 (100)
Total, n (%)	25 (13.44)	67 (36.02)	94 (50.54)	186 (100)

58%) in the MRD group (HD versus MUD, P = .6; HD versus MRD, P = .8) (Table 3; Supplementary Table 1). MVA revealed no difference in PFS among the 3 donor groups. Patients with HL had better PFS (HR, .5; 95% CI, .3 to .9; P = .01), wheres patients receiving >3 previous lines of chemotherapy had worse PFS (HR, 1.8; 95% CI, 1.2 to 2.6; P = .01). None of the other factors evaluated was associated with PFS (Figure 1).

In univariate analysis, OS at 3 years was 52% (95% CI, 28% to 71%) in the HD group, 54% (95% CI, 44% to 64%) in the MUD group, and 67% (95% CI, 54% to 77%) in the MRD group (HD versus MUD, P = .9; HD versus MRD, P = .2) (Table 3; Supplementary Table 1). There were no significant predictors of OS on MVA.

The 3-year GRFS rate tended to be higher in the HD group (45%; 95% CI, 22% to 65%; reference) compared with the MUD (34%; 95% CI, 25% to 43%; P = .3) and MRD (29%; 95% CI, 18% to 41%; P = .2) groups (Figure 2), yet these differences did not reach statistical difference. Causes of death in all donor groups are listed in Supplementary Table 2.

Comparison of the FM100 and FM140 Conditioning Regimens

Compared with the FM140 conditioning regimen, the FM100 regimen was more likely to be used in older patients (median age, 57 years versus 46 years; $P < .01$) and in patients in the HD group (64% versus 11%; $P < .01$). Consequently, patients receiving an FM100 regimen were also more likely to

Table 3
Univariable Analysis for Outcomes by Donor Type

Outcomes	HD (N = 25)	MUD (N = 98)	MRD (N = 63)	*P* Value
Relapse rate, %				HD (reference)
3-yr incidence	15	21	39	HD vs MUD, .4
95% CI	5-42	14-31	29-54	**HD vs MRD, .04**
NRM, %				HD (reference)
3-yr incidence	31	32	10	HD vs MUD, .9
95% CI	16-58	24-43	4-20	**HD vs MRD, .02**
PFS, %				HD (reference)
3-yr incidence	49	44	46	HD vs MUD, .6
95% CI	26-69	34-54	33-58	HD vs MRD, .8
OS, %				HD (reference)
3-yr incidence	52	54	67	HD vs MUD, .9
95% CI	28-71	44-64	54-77	HD vs MRD, .2
aGVHD grade II-IV, %				HD (reference)
6-mo incidence	29	36	35	HD vs MUD, .4
95% CI	16-55	28-47	25-49	HD vs MRD, .5
aGVHD grade III-IV, %				HD (reference)
6-mo incidence	4	14	8	HD vs MUD, .2
95% CI	1-28	8-23	3-18	HD vs MRD, .5
cGVHD, %				HD (reference)
3-yr incidence	5	16	26	HD vs MUD, .2
95% CI	1-36	10-26	17-42	**HD vs MRD, .09**
GRFS, %				HD (reference)
3-yr incidence	45	34	29	HD vs MUD, .3
95% CI	22-65	25-43	18-41	HD vs MRD, .2
3-yr PFS by disease type, % (95% CI)				
NHL	42 (15-67)	31 (19-44)	41 (24-58)	
HL	50 (6-84)	60 (42-75)	56 (32-74)	
CLL	75 (13-96)	50 (24-71)	41 (14-67)	
3-yr OS by disease type, % (95% CI)				
NHL	42 (15-67)	42 (28-55)	62 (42-77)	
HL	67 (5-94)	73 (54-85)	78 (51-91)	
CLL	75 (13-96)	56 (29-76)	60 (28-81)	

Significant *P* values are in bold type.

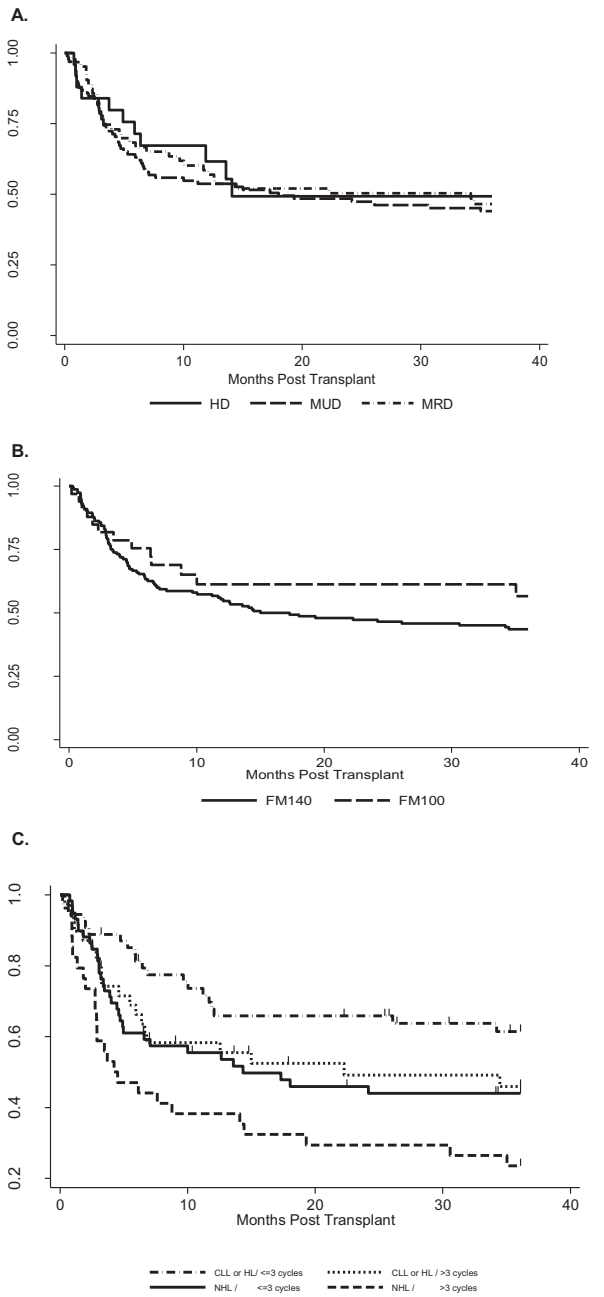

Figure 1. PFS by donor type (A), melphalan dose (B), and disease and number of chemotherapy cycles received (C).

receive a BM graft (55% versus 25%; $P = .01$). In univariate analysis, the FM100 and FM140 regimens had similar outcomes in terms of PFS (HR, .7; $P = .3$), relapse rate (HR, .4; $P = .1$), and NRM (HR, .9; $P = .8$). The 3-year PFS was 57% in patients receiving FM100 43% in those receiving FM140 ($P = .3$), and the corresponding 3-year OS in the 2 groups was 64% versus 58% ($P = .7$).

DISCUSSION

Here we evaluated the impact of donor type and melphalan dose on outcomes in patients with lymphoma who underwent an FM-based conditioning regimen and ASCT at our institution. This analysis shows comparable survival after HD-ASCT, MUD-ASCT, and MRD-ASCT. Compared with the MRD group, the HD group had a lower relapse rate but higher NRM, which

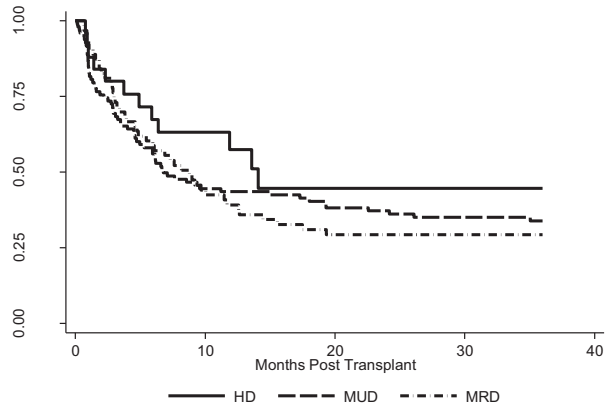

Figure 2. GRFS by on donor type.

appeared to offset the benefit and yielded similar survival. The rate of cGVHD was significantly lower in the HD group, whereas other outcomes were similar in the HD and MUD groups. In addition, we showed that the nonmyeloablative FM100 regimen, although used in significantly older patients and patients with comorbidities, was not inferior in terms of survival compared with the more intense myeloablative FM140 regimen, and, notably, the FM140 regimen was not associated with a lower relapse rate.

FM-based conditioning regimens remain some of the most widely used conditioning regimens for ASCT for lymphoma [22]. More recently, our group began using lower doses of melphalan (FM100) for older individuals and observed comparable outcomes with the FM100 and FM140 regimens for patients with acute leukemia and multiple myeloma [23,24]. We found similar results in patients with lymphoma. A previous phase II trial evaluated the FM100 regimen in 26 lymphoma patients, 20 of whom (77%) had progressive disease at the time of ASCT [25]. The 5-year OS and NRM rates were 40.4% and 21.2%, respectively, with no adverse effect on engraftment. In our study, despite the higher proportion of older patients or with significant comorbidities, survival was comparable in the FM100 and FM140 groups (3-year OS, 64% versus 58%), confirming our initial observations [18] and raising the question of whether FM100 conditioning should replace FM140 conditioning for all patients with lymphoma to further decrease NRM in younger patients and possibly improve survival.

Recently, the Center for International Blood and Marrow Transplant Research published 2 large retrospective series comparing outcomes of HD-ASCT with those of MUD and MRD ASCTs in patients with lymphoma [9,17]. The first report compared 185 HD-ASCT recipients who received PTCy GVHD prophylaxis with 807 MRD-ASCT recipients who received calcineurin-based GVHD prophylaxis [17]. There were no differences in post-transplantation outcomes between the 2 groups, but HD-ASCT was associated with a significantly lower risk of cGVHD. In our cohort, as reported previously [20], the use of an FM/TBI regimen compared with F/Cy/TBI in the foregoing series was associated with a higher NRM (34% versus 15%) but a lower relapse rate (15% versus 40%) in HD-ASCT, resulting in a similar PFS (48% versus 49%). These results suggest that younger and fit patients should be offered a FM100/TBI regimen owing to the lower risk of relapse, whereas older patients or those with significant comorbidities might benefit more from a F/Cy/TBI regimen, which is associated with the lowest NRM.

In the second report [9], a comparison of 732 MUD-ASCT recipients and 185 HD-ASCT recipients who received PTCy showed comparable outcomes in the 2 donor groups except for significantly lower rates of aGVHD and cGVHD in the HD-ASCT group. Multiple studies comparing HD-ASCT with PTCy GVHD prophylaxis with MUD-ASCT performed with standard calcineurin-based GVHD prophylaxis have consistently shown better GVHD control and a plateau in OS after 2 years, owing to decreased mortality from cGVHD in HD ASCT groups. These observations suggest that patients receiving an HLA-matched donor transplant could also benefit from PTCy-based GVHD prophylaxis. The ongoing Blood and Marrow Transplant Clinical Trials Network trial 1203 evaluating PTCy as GVHD prophylaxis in ASCT will provide more insight into the impact of PTCy in this setting. In addition, given the ease of donor availability in HD-ASCT and comparable outcomes to those in MUD-ASCT, patients—especially those who require urgent disease control (ie, those who fail to respond to chemotherapy, achieve partial response, or fail chimeric antigen receptor T cell therapy)—should proceed immediately to HD-ASCT. This could bring more patients to transplantation and provide an opportunity for cure for these patients who otherwise are bound to have dismal outcomes. This approach appears to be reflected in the fact that the number of HD transplantations continues to increase worldwide, compared with MUD transplantations, the rate of which has appeared to have plateaued in recent years [12].

Another interesting observation in our analysis was an impressive 3-year OS of 78% in patients with HL even though most patients in our cohort had advanced disease. Although the number of patients in our cohort is too small to allow us to draw firm conclusions, a lower relapse rate with HD-ASCT in patients with HL is possible, as has been reported by others [7,8].

Limitations of this study are related to the relatively small number of patients and heterogeneity of disease type, even though the same conditioning regimen was used in all patients. However, we confirm similar outcomes in HD and HLA-matched donor transplants in a group of patients treated with the same conditioning regimen, suggesting that PTCy-based GVHD prophylaxis should be extended to all donor types, and that reduced melphalan doses likely should be used in all patients.

In conclusion, our study adds to the growing literature from multiple centers and registries lending support to the feasibility of HD-ASCT as an attractive alternative to HLA-matched donor ASCT for patients with lymphoma and perhaps the preferential use of an HD for patients who cannot wait for an MUD. Stratification for treatment of patients with lymphoma—at least for those undergoing HD-ASCT—might be necessary based on conditioning intensity. Younger and more fit patients who can tolerate a more intensive regimen might benefit from an FM100/TBI regimen owing to a lower rate of relapse, whereas older patients and patients with comorbidities might benefit from lower-intensity conditioning, such as an F/Cy/TBI regimen, which has been associated with the lowest NRM [8]. FM140-based conditioning does not appear to provide any added benefit for any group of patients. Future randomized studies could provide insight into which reduced-intensity regimen is superior for patients with lymphoma. Moreover, these results, in conjunction with the recent literature, also suggest that RIC ASCT, perhaps in conjunction with immunotherapy or maintenance therapy, should replace more intensive conditioning for patients with lymphoma.

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SUPPLEMENTARY DATA

Supplementary data related to this article can be found online at doi:10.1016/j.bbmt.2019.02.002.

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