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Clinical outcomes of allogeneic stem cell transplantation for relapsed or refractory follicular lymphoma: a retrospective analysis by the Fukuoka Blood and Marrow Transplantation Group

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Abstract

Allogeneic hematopoietic stem cell transplantation (allo-SCT) is considered as the only curative treatment for relapsed or refractory follicular lymphoma (FL), but it has a high treatment-related mortality rate. Only a few reports, however, have described the efficacy of allo-SCT for FL in the Japanese population. We have retrospectively analyzed the outcome of allo-SCT in 30 patients with FL. Seventeen (56.7%) patients were chemorefractory, whereas 13 (43.3%) were chemosensitive. An estimated 2-year overall survival rate (OS) and relapse rate of all patients 46.7% and 20.0%, respectively. There were no significant differences in the estimated 2-year OS rate between patients who received myeloablative conditioning and those who received reduced-intensity conditioning (P = 0.98), and among the recipients of related bone marrow (BM) / peripheral blood stem cell, unrelated BM and umbilical cord blood (P = 0.20). In patients who were either chemosensitive or chemorefractory at allo-SCT, the 2-year OS rate was 69.2% and 29.4% (P = 0.06). Patients with mild-to moderate acute GVHD had better the 2-year PFS rate compared with patients who had severe acute GVHD (P=0.01), but not better PFS compared with patients who had no acute GVHD (P=0.12). Our results suggest that the graft-versus-lymphoma effects of allo-SCT may provide survival benefits even in patients with chemorefractory FL.

Introduction

Although follicular lymphoma (FL) responds well to first-line therapy, relapses requiring therapeutic interventions are common, with disease-free intervals becoming progressively shorter [1,2]. Allogeneic hematopoietic stem cell transplantation (allo-SCT) can result in long-term control of FL, in part, through the graft-versus-lymphoma (GVL) immune response [3,4]. A comparative retrospective study revealed a significantly lower relapse rate in patients with relapsed FL who underwent allo-SCT compared with those who underwent autologous SCT (auto-SCT) or salvage chemotherapy [5,6]. Therefore, allo-SCT has become the treatment of choice for patients with relapsed or refractory FL [7,8]. However, the potential survival benefits of allo-SCT compared with that of auto-SCT is often offset by the high treatment-related mortality (TRM) rate, due to direct toxicity and high incidence of severe graft-versus-host disease (GVHD). Recently, the use of reduced-intensity conditioning (RIC) regimen has become standard practice in older patients or those with comorbid physical conditions to decrease the TRM rate of allo-SCT. In addition, umbilical cord blood (UCB) is increasingly preferred for patients who do not have access to a human leukocyte antigen (HLA)-matched donor because of the availability of stored transplantable units and the lower risk of GVHD, thus permitting less stringent HLA matching. Because of these advances, allo-SCT is rapidly being adopted for patients with FL requiring allo-SCT. However, only few reports have described the efficacy of allo-SCT for FL in the Japanese population [8-10].

In this study, we retrospectively analyzed the clinical outcomes of 30 Japanese patients with FL who underwent allo-SCT between 1997 and 2010 using different graft sources including bone marrow (BM), peripheral blood stem cell (PBSC), and UCB. This is the era after the introduction of rituximab, but prior to the availability of the alkylating agent, bendamustine [11]. Radioimmunoconjugated drug ^{90}Y-ibritumomab tiuxetan [12] was available since 2008 in Japan, but no patients had been treated by ^{90}Y-ibritumomab tiuxetan prior to allo-SCT in our study. On the basis of our observations and previously reported literatures, we have

discussed the implications of our findings on the role of allo-SCT in the new drug era for FL treatment.

Patients and methods

Patient Characteristics

Between 1997 and 2010, 30 patients (males, 15; females, 15; median age, 52 years; range, 32–65 years) with relapsed or refractory FL who underwent allo-SCT at four of the Fukuoka Blood and Marrow Transplantation Group institutions were enrolled in this study (Table 1). The World Health Organization (WHO) criteria were used for the diagnosis of FL [13]. The median duration from diagnosis to transplantation was 38.5 months (range, 4–122), the median follow-up duration was 21.4 months in all of the patients (range, 0.4–165.4), and the median follow-up duration of surviving patients was 57.1 months (range 27.8–165.4). All patients underwent chemotherapy in combination with rituximab prior to allo-SCT; the median number of previous chemotherapy regimen was four (range, 2–8), and two patients had received high-dose chemotherapy and autologous peripheral blood stem cell transplantation (PBSCT). Only five patients underwent re-biopsy before allo-SCT. All of the five patients demonstrated progression of degree of FL grade and one of the patients progressed to diffuse large B-cell lymphoma. In our study, re-biopsy rate was low (17%); therefore, there was a possibility to include patients with histologic transformation to more aggressive lymphoma. Response criteria were based on guidelines from the international workshop on non-Hodgkin's lymphoma [14]. At the time of allo-SCT, four patients were in complete remission (CR), nine in partial remission (PR), and 17 in progressive disease (PD).

Conditioning Regimen and Graft-versus-Host Disease Prophylaxis

The conditioning regimens included myeloablative conditioning (MAC) in 13 patients and RIC in 17 patients. MAC regimens included intravenous busulfan and cyclophosphamide (Bu and CY; 12.8 mg/kg and

120mg/kg, respectively) in 2 patients; Bu and melphalan (Bu and L-PAM; 16 mg/kg oral and 200 mg/m^2 intravenous, respectively) in 1 patient; total body irradiation (TBI) plus intravenous CY (TBI and CY; 12Gy and 120 mg/kg, respectively) or TBI/CY plus either intravenous etoposide or thiotepa in 10 patients. RIC, with or without low-dose TBI (2–4 Gy), included intravenous fludarabine and Bu in 10 patients [Flu/Bu; either 125–180 mg/m^2 plus Bu 16 mg/kg oral or 6.4 mg/kg intravenous with or without low-dose TBI (2–4 Gy) , respectively]; intravenous Flu/L-PAM, in 5 patients [125–180 mg/m^2 and 140 mg/m^2 intravenous with or without low-dose TBI (2–4 Gy), respectively], and 2 received other regimens such as rituximab, cladribine and L-PAM (Table 1). In the MAC group, median age at allo-SCT was 50 years (range, 32–56) with 7 patients aged >50 years. In the RIC group, median age at allo-SCT was 53 years (range, 47–65) with 13 patients aged >50 years; patients in the RIC group were significantly older than those in the MAC group ($P < 0.01$). None of the patients in the MAC group had undergone an auto-SCT prior to allo-SCT compared with two patients in the RIC group. At the time of allo-SCT, four patients in the MAC group, and nine patients in the RIC group were chemosensitive (CR+PR) (Table 1); this difference was not statistically significant ($P = 0.11$).

Related bone marrow transplantation (BMT) was performed in three patients, related PBSCT in 10, unrelated BMT in 12, and unrelated umbilical cord blood transplantation (UCBT) in five (Table 1). GVHD prophylaxis included cyclosporine (n = 15) and tacrolimus (n =15) combined with methotrexate or mycophenolate mofetil as described previously [15,16]. None of the patients received anti-thymocyte globulin during the conditioning regimen.

Assessment of Engraftment, GVHD and Survival

Engraftment was defined as an absolute neutrophil count of more than 0.5×10^9/L for three consecutive days. Acute and chronic GVHD were diagnosed and graded according to the standard criteria described previously [17-19]. Overall survival (OS) rate was computed from the date of transplantation.

Statistical Analysis

The probability of survival was estimated using the Kaplan–Meier method [20]. The effects on survival in patient and disease variables were examined using the log-rank test. In addition, because the risk of chronic GVHD (cGVHD) usually begins by day 50 following allo-SCT, we performed a "landmark" analysis, 50 days after allo-SCT, of OS rate relative to the GVHD grade [21].

Results

Engraftment

Twenty-six patients achieved engraftment, and the median time for neutrophil count recovery was 16 days (range 10–29 days) following allo-SCT. Engraftment was not analyzed in 3 patients (1 BM, 1 PBSC, and 1 UCB recipient) because of fatal disease progression (n = 1), sinusoidal obstruction syndrome (SOS; n = 1), or thrombotic microangiopathy (TMA; n = 1). Primary engraftment failure occurred in one UCB recipient.

Graft-versus-Host Disease

Of the 26 evaluable patients, 17 (65.4%) developed acute GVHD (aGVHD), including nine patients (34.6%) with grade I disease, four patients (15.4%) with grade II disease, and four patients (15.4%) with grade III–IV disease (Table 2). Fifteen (60.0%) of the 25 patients who survived longer than 50 days developed cGVHD, which was limited in four and extensive in 11 (Table 2). None of the patients received a donor lymphocyte infusion.

Survival

With the median follow-up of 21.4 months, the Kaplan–Meier estimate of total OS and

progression free survival (PFS) rates at 2 years were 46.7% and 46.7%, respectively, with 15 patients being disease-free (Figure 1a). There was no significant difference in the estimated 2-year OS rate in patients who underwent MAC (46.2%, n = 13) and RIC (47.1%, n = 17) (P = 0.98; Figure 1b). In the related BM/PBSC (n = 13), unrelated BM (n = 12), and UCB (n = 5), the estimated 2-year OS rate were 38.5%, 66.7%, and 20.0%, respectively (UCB vs. unrelated BM; P = 0.20; Figure 1c). In patients who were either chemotherapy-sensitive (CR + PR) or chemorefractory at allo-SCT, the estimated 2-year OS was 69.2% and 29.4%, respectively (P = 0.06; Figure 1d).

Effects of Graft-versus-Host Disease on Survival and Mortality

Further, we compared survival rates relative to the severity of aGVHD in 26 patients. Two-year PFS was estimated to be 44.4%, 76.9%, and 0% in patients with grade 0, I–II, or grade III–IV aGVHD, respectively (Figure 2a). PFS at 2 years was shorter in the patients with grade III–IV than those with either grades 0 or I–II (P = 0.03 and P < 0.01, respectively). There was no significant difference in the 2-year PFS rate between the patients with grade 0 and I–II aGVHD (P = 0.12). The cause of death according to the grade of aGVHD is summarized in Table 2. The main cause of death among patients without aGVHD (n = 9) and those with grade III–IV (n = 4) were cGVHD (n = 2; 22.2%) and aGVHD (n = 3; 75.0%), respectively. In patients with grade I–II aGVHD (n = 13), specific cause of death was not observed.

In the 25 patients who survived for longer than 50 days after allo-SCT, there were no significant differences in the estimated 2-year PFS rate among the patients who developed or did not develop cGVHD (None ; 40.0%, Limited ; 75.0%, Extensive ; 63.6% ; P = 0.44) (Figure 2b). The cause of death according to the grade of cGVHD is summarized in Table 2. The main cause of death among patients without cGVHD (n = 10) and those with extensive cGVHD (n = 11) were relapse (n = 3; 30.0%) and cGVHD (n = 3; 27.3%), respectively. In patients with limited cGVHD (n = 4), specific cause of death was not observed. In patients

who developed cGVHD, relapse was not observed.

Relapse, TRM and Causes of Death

Four patients (13.3%) exhibited disease progression after allo-SCT (median 90 days; range, 11–593 days) and died because of the underlying disease. The treatment-related mortality rates and relapse rate at 2year were 33.3% and 20.0%, respectively. Of 17 patients who suffered from treatment-related deaths, 6 patients died of GVHD: acute GVHD in 3 patients, chronic GVHD in 3 patients. The other cause of death was SOS/TMA in 2, multiple organ failure in 1, acute pancreatitis in 1, interstitial pneumonitis in 1, invasive pulmonary aspergillosis after second UCBT in 1, and sudden death in 1.

Discussion

FL is a slow, progressive B-cell malignancy with a median survival time of 8–10 years from diagnosis. Although the availability of rituximab has improved both the outcome and survival of FL [22,23], patients with relapsed or refractory FL are advised to undergo allo-HSCT before they receive excessive chemotherapies and their physical condition is exacerbated by the adverse effects. The previous reports of allo-SCT for relapsed and refractory FL are summarized in Table3 [8,24-32]. PFS and OS rates among the patients who received allo-SCT with RIC varied between approximately 40% and 80%, which was almost equivalent to those of our result. Two large registry studies from the Center for International Blood and Marrow Transplant Research (CIBMTR) and the European Group for Blood and Marrow Transplantation (EBMT) on patients with relapsed FL revealed that myeloablative allo-SCT has a significantly lower rate of relapse than auto-SCT; however, both transplants have similar long-term OS rates (50–62% at 4–5 years) because of a 30–38% increase in the TRM rate in patients who underwent allo-SCT [32,33]. On the basis of these results, allo-SCT with RIC regimen is recognized as one of the promising conditioning regimens due to

its reduced non-relapse mortality (NRM) rate and effective GVL effect.

Several studies have shown that FL is highly sensitive to the GVL effect, making allo-SCT a promising treatment modality with curative potential for relapsed or chemotherapy-resistant FL [4,34]. Although the development of severe GVHD is associated with poor outcome, mild-to-moderate aGVHD may confer a lower risk of disease progression and be beneficial for survival after allo-SCT for acute myeloid leukemia, chronic myelogenous leukemia, and adult T-cell leukemia/lymphoma [35-37]. In our study, the 2-year PFS rate was superior in patients who developed mild-to-moderate aGVHD than in those who developed either no aGVHD or severe aGVHD and relapse was not observed in the patients with cGVHD. The impact of GVHD on clinical outcomes after allo-SCT or FL remains unknown. However, the previous study showed excessive GVHD prophylaxis such as T-cell depletion caused a higher relapse rate [38]. These results suggested that mild-to-moderate aGVHD and cGVHD may have a beneficial influence on survival via GVL effects. However, further large-scale studies are required to assess the impact of acute and chronic GVHD on survival of patients with FL.

The reduced risk of relapse following MAC conditioning with allo-SCT offset by NRM associated with an intensive preparative regimen. Therefore, the use of allo-SCT following RIC is gradually increasing for patients with relapsed or refractory FL who are coping with comorbid physical conditions caused by disease progression and repeated chemotherapy. Two large registry studies have compared the outcomes of patients with FL who underwent allo-SCT following either RIC or MAC. The CIBMTR study found no difference in the 3-year PFS rate (RIC, 55% vs. MAC, 67%, $P = 0.07$) or the 3-year OS rate (RIC, 62% vs. MAC, 71%, $P = 0.15$) in 208 patients with FL, even though their analysis was limited to recipients of matched-related donors [25]. The EBMT study had 131 patients with solely unrelated donor grafts. In contrast to the CIBMTR study, the EBMT study found that recipients of the RIC regimens had a lower NRM and experienced a significantly improved PFS and OS by multivariate analysis [26]. However, in both the

CIBMTR and EBMT studies, chemoresistance and a lower performance status were found to affect TRM, OS, and PFS rates adversely. In our report, we also found no significant difference while comparing the 2-year OS rates between patients in the RIC and MAC groups (47.1% vs. 46.2%, respectively; P = 0.98). In contrast, the 2-year OS rate was superior in chemosensitive patients (CR+PR) compared with those in the chemorefractory group (69.2% vs. 29.4%, respectively; P = 0.06). The *Grupo Español de Linfomasl/Tranplante de Médula Osea* group reported significant differences in the 4-year DFS rate for 37 patients with FL who were treated by reduced-intensity stem cell transplantation (RIST) conditioning with progressive disease (PD), PR, or CR at allo-SCT (29%, 48%, and 64%, respectively; P = 0.02), whereas the 4-year cumulative incidence of NRM was 71%, 33%, and 26%, respectively (P = 0.04) [29]. In addition, the French Society of Bone Marrow Graft Transplantation and Cellular Therapy group reported that the 3-year DFS rate in 73 patients with FL who were treated by RIST conditioning with PD, PR or CR at allo-SCT was 32%, 52%, and 66%, respectively (P = 0.003), whereas the 3-year cumulative incidence of NRM was 63%, 28%, and 32%, respectively (P = 0.005) [39]. These data show that chemosensitivity at the time of allo-SCT, and not the conditioning intensity, is more reliable predictor of FL outcome in recipients of allo-SCT, and suggested that allo-SCT using RIC for relapsed FL may result in long-term surviving for some but significant proportion of patients with chemoresistant disease.

Recent trails have focused on how to incorporate novel molecular targeted agents into the allo-SCT conditioning regimen with the intention increasing the anti-lymphoma activity and decreasing toxicity. The M.D. Anderson group reported the outcome of patients with relapsed FL receiving allo-SCT in combination with a high-dose of rituximab, Flu, and CY [24]. Radioimmunotherapies, such as ^{90}Y-ibritumomab tiuxetan, confer cytoreduction via targeted delivery of radiation with isotopes-conjugated monoclonal antibodies. The M.D. Anderson group also reported the outcomes for 26 patients with relapsed FL who were treated with RIC and allo-SCT using ^{90}Y-ibritumomab tiuxetan in combination with Flu and CY

[24]. The 3-year PFS rate for chemorefractory or chemosensitive patients were 80% and 87%, respectively, whereas the 1-year TRM rate was only 8%. The M.D. Anderson group also reported the results of combining allo-SCT with bendamustine in 16 patients with lymphoma. After a median follow-up period of 6 months, the OS and PFS rates for 16 patients with mantle cell lymphoma, FL, chronic lymphocytic leukemia and diffuse large B-cell lymphoma were 87% and 78%, respectively [40]. Based on these results, it is feasible to incorporate novel agents into the allo-SCT regimens because of the acceptable TRM rates and promising efficacy in patients with chemorefractory FL.

In conclusion, our results revealed that allo-SCT was the only treatment that could result in long-term survival even for chemorefractory group, since GVHD may confer a beneficial influence on survival. Although allo-SCT possesses a GVL effect, it is also associated with severe TRM rates. Treatment of FL is now being further refined by bendamustine as the chemotherapy backbone and by determining the role of rituximab maintenance and radioimmunotherapy consolidation. Incorporating these novel agents into salvage chemotherapy before allo-SCT and / or conditioning regimen may improve the outcome of allo-SCT. Further large-scale studies are required to assess the efficacy and safety of allo-SCT in the era of these novel agents for patients with chemorefractory FL.

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Figure Legends

Figure 1. Kaplan–Meier estimates of (a) OS and PFS rates in all FL patients (n = 30); (b) OS rates according to intensity of conditioning regimen; (c) OS rates according to stem cell source; (d) OS rates according to chemosensitivity at transplantation.

Figure 2. Kaplan–Meier estimates of the PFS rates according to (a) the grade of acute GVHD (excluding four cases of early death); (b) the grade of chronic GVHD in 25 patients who survived longer than 50 days after transplantation.

Figure 1.

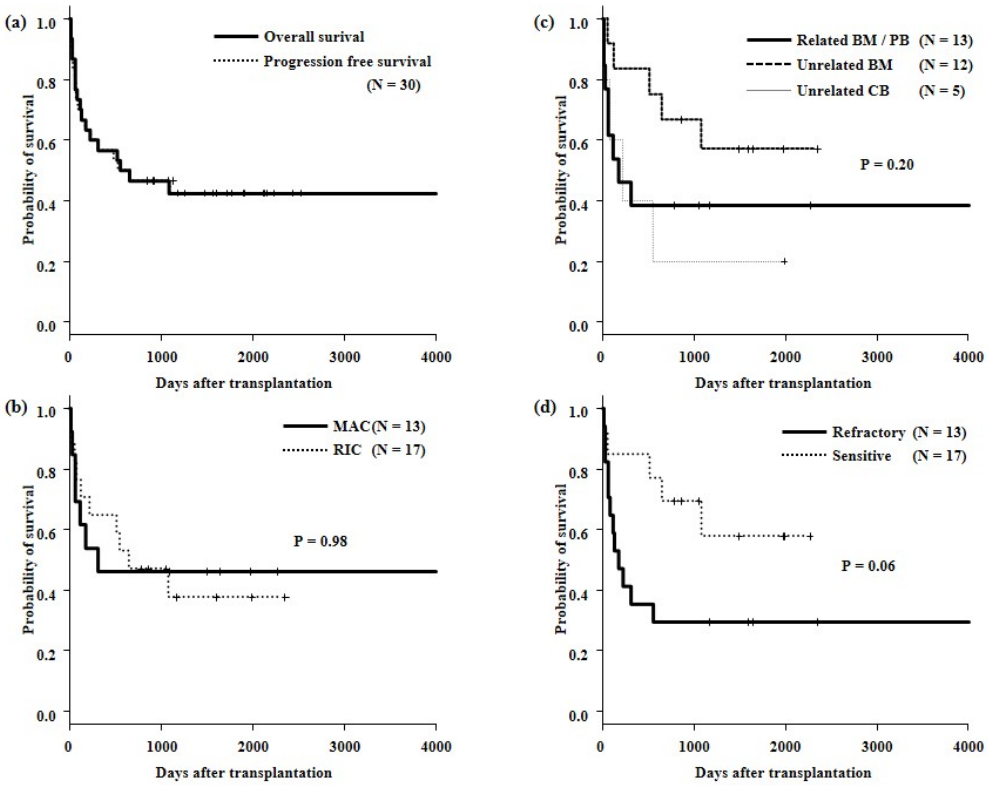
(a)
Overall surival
Progression free survival
(N = 30)
Probability of survival
Days after transplantation
(b)
MAC(N = 13)
RIC (N = 17)
P = 0.98
Probability of survival
Days after transplantation
(c)
Related BM / PB (N = 13)
Unrelated BM (N = 12)
Unrelated CB (N = 5)
P = 0.20
Probability of survival
Days after transplantation
(d)
Refractory (N = 13)
Sensitive (N = 17)
P = 0.06
Probability of survival
Days after transplantation

Figure 2.

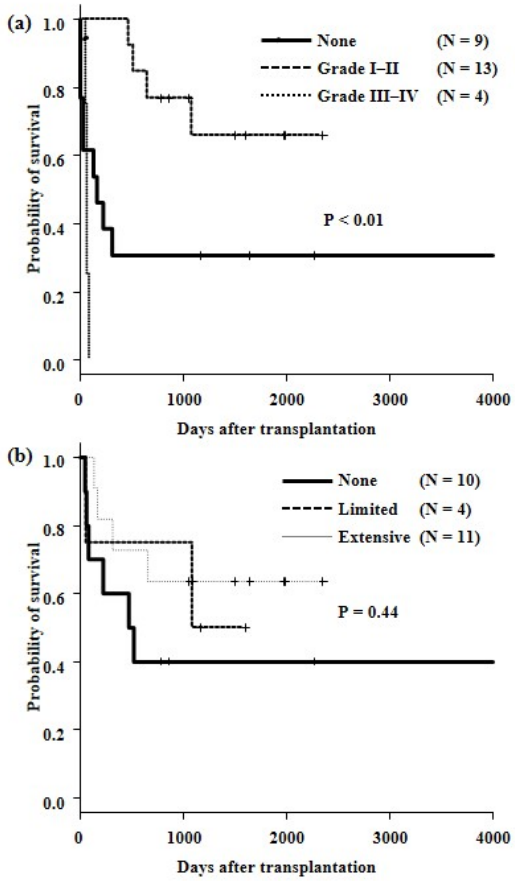
(a)
None (N = 9)
Grade I–II (N = 13)
Grade III–IV (N = 4)
P < 0.01
Probability of survival
Days after transplantation
(b)
None (N = 10)
Limited (N = 4)
Extensive (N = 11)
P = 0.44
Probability of survival
Days after transplantation

Table 1. Patient and Disease Characteristics

Characteristics	Total (N=30)	MAC (N=13)	RIC (N=17)	P value
Sex				
Male / Female	15 / 15	8 / 5	7 / 10	0.13
Age, years				
Median (range)	52 (32-65)	50 (32-56)	53 (47-65)	<0.01
<50	11	6	4	
≧50	20	7	13	
Time from diagnosis to transplant, months				
Median (range)	38.5 (4-122)	26 (4-122)	42 (8-120)	0.06
Previous treatment				
Previous chemotherapy lines				0.02
Median (range)	4 (2-8)	2 (2-5)	4 (2-8)	
2	9	8	1	
3	5	2	3	
4	6	1	5	
5	7	2	5	
6–8	3	0	3	
Previous autograft	2	0	2	
Stem cell source				<0.01
Related BMT/PBSCT	13	9	4	
Unrelated BMT	12	4	8	
UCBT	5	0	5	
Conditioning regimen		TBI/CY ± α; 10 Bu/CY; 2 Bu/L-PAM; 1	Flu/Bu ± TBI; 10 Flu/L-PAM ± TBI; 5 Rit/CdA/L-PAM; 1 TBI/thiotepa/CY; 1	
Disease status at allo-SCT				0.11
Chemosensitive	13	4	9	
CR	4	1	3	
PR	9	3	6	
Chemorefractory	17	9	8	

Abbreviations

MAC, myeloablative conditioning; RIC, Reduced-intensity conditioning; BMT, bone marrow transplantation; PBSCT, peripheral blood stem cell transplantation; UCBT, umbilical cord blood transplantation; TBI, total body irradiation; CY, cyclophosphamide; Bu, busulfan; L-PAM, melphalan; Flu, fludarabine; Rit, rituximab; CdA; cladribine; allo-SCT, allogeneic hematopoietic stem cell transplantation; CR, complete remission; PR, partial remission

Table 2. Cause of death according to the grade of acute and chronic GVHD

Acute GVHD[*1]	None (n = 9)	I–II (n = 13)	III–IV (n = 4)	Total (n = 26)
Dead (%)	5 (55.5)	4 (30.8)	4 (100.0)	13 (50.0)
Cause of death				
Relapse (%)	1 (11.1)	1 (7.7)	1 (25.0)	3 (11.5)
aGVHD (%)	0 (0.0)	0 (0.0)	3 (75.0)	3 (11.5)
cGVHD (%)	2 (22.2)	1 (7.7)	0 (0.0)	3 (11.5)
Others (%)	2 (22.2)	2 (15.4)	0 (0.0)	4 (15.4)
Chronic GVHD[*2]	None (n =10)	Limited (n = 4)	Extensive (n =11)	Total (n = 25)
Dead (%)	6 (60.0)	2 (50.0)	4 (36.4)	12 (48.0)
Cause of death				
Relapse	3 (30.0)	0 (0.0)	0 (0.0)	3 (12.0)
aGVHD	2 (20.0)	1 (25.0)	0 (0.0)	3 (12.0)
cGVHD	0 (0.0)	0 (0.0)	3 (27.3)	3 (12.0)
Others	1 (10.0)	1 (25.0)	1 (9.1)	3 (12.0)

Abbreviations

GVHD, graft-versus-host disease survival

[*1] except four cases of graft failure

[*2] patients who survived longer than 50 days after allo-SCT

Table 3. Previous reports of allogeneic stem cell transplantation for relapsed follicular lymphoma

Study	N	Median age, y (range)	Donor	Prior auto-SCT	Dose intensity	Conditioning regimen	Status at allo-SCT, Chemoresistant, no	PFS	OS	TRM	Median follow-up
M.D.Anderson [24]	47	53 (33-68)	MRD URD	19%	RIC	Flu/CY/Rit	0 (0%)	72% (11y)	78% (11y)	21%	107 mo
	26	55 (26-66)	MRD URD	0%	RIC	Flu/CY/^{90}Y	10 (38%)	85% (3y)	88% (3y)	8%	33 mo
CIBMTR [25]	120	44	MRD	6%	MAC	Various	27 (23%)	67% (3y)	71% (3y)	25%	82 mo
	88	51	MRD	10%	RIC	Various	23 (26%)	55% (3y)	62% (3y)	28%	54 mo
EBMT [26]	44	42	URD	23%	MAC	Various	15 (34%)	43% (3y)	47% (3y)	37%	38 mo
	87	51	URD	59%	RIC	Various	20 (23%)	49% (3y)	53% (3y)	33%	34 mo
CALGB [27]	44 (16 with FL)	53 (39-68)	MRD	0%	RIC	Flu/CY	0 (0%)	75% (3y)	81% (3y)	9%	4.6 y
United Kingdom [28]	82	45 (26-65)	MRD URD	26%	RIC	Flu/L-PAM/Alem	7 (9%)	76% (4y)	76% (4y)	15%	43 mo
GELTAMO [29]	37	50 (34-62)	MRD	46%	RIC	Flu/L-PAM	7 (19%)	57% (4y)	54% (4y)	37%	52 mo
FHCRC [30]	62 (54 with FL)	54 (33-66)	MRD URD	32%	RIC	TBI±Flu	23 (37%)	43% (3y)	52% (3y)	42%	36 mo
Keio uinv [8]	19	47 (34-58)	MRD URD	11%	RIC	Flu/L-PAM±TBI	13 (68%)	84% (5y)	84% (5y)	16%	75 mo
IBMTR [31]	176	42 (22-64)	MRD	NA	MAC	Various	39 (37%)	45% (3y)	51% (3y)	30%	36 mo
EBMT [32]	231 (low-grade NHL)	39 (19-66)	MRD URD	NA	MAC	Various	42 (20%)	43% (4y)	51% (4y)	38%	60 mo
FBMTG	17	53 (47-65)	RD URD CB	12%	RIC	Various	9 (69%)	47% (2y)	47% (2y)	41%	23 mo
	13	50 (32-56)	RD URD	0%	MAC	Various	8 (47%)	46% (2y)	46% (2y)	23%	11 mo

Abbreviation

CALGB, Cancer and Leukemia Group B; CIBMTR, Center for International Blood and Marrow Transplant Research; GELTAMO, Grupo Español de Linfomasl/Tranplante Autólogo de Médula Ósea; FHCRC, Fred Hutchinson Cancer Research Center; FBMTG, Fukuoka Bone Marrow Transplantation Group; IBMTR, International Bone Marrow Transplant Registry; NA, not applicable; FL, follicular lymphoma; NHL, non-Hodgkin lymphoma; MRD, matched related donor; URD, unrelated donor; RD, related donor; CB, cord blood donor; RIC, reduced-intensity conditioning; MAC, myeloablative conditioning; Flu, fludarabine; CY, cyclophosphamide; Rit, rituximab; ^{90}Y, ^{90}Y-ibritumomab tiuxetan; L-PAM, melphalan; Alem, alemtuzumab; TBI, total body irradiation; PFS, progression free survival; OS, overall survival; TRM, treatment related mortality;

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