of 3 consecutive days after transplantation that the absolute neutrophil count exceeded 0.5×10^9/L of peripheral blood. The diagnosis and clinical grading of acute and chronic GVHD (aGVHD, cGVHD) were performed according to established criteria [22-24]. CR was defined as lower than 5% blasts in the bone marrow, with a neutrophil count $>1.5 \times 10^9$/L and a platelet count $>100 \times 10^9$/L in leukemia/MDS patients, and according to the International Workshop Criteria [25] in lymphoma patients.

Statistical Analysis

The endpoints of the study were progressive disease/relapse (PD), NRM, overall survival (OS), and progression-free survival (PFS). OS, NRM, and PD were defined as the time between stem cell infusion to the event. PFS was defined as the time between stem cell infusion to PD or death from any cause, whichever occurred earlier. OS and PFS were estimated by the Kaplan-Meier method [26]. NRM and PD were estimated by the cumulative incidence. The chi-square test or Fisher's exact test was used to evaluate the differences in the clinical characteristics of the CST and RIST groups. The log-rank test and the generalized Wilcoxon test were used to compare the probabilities of survival, NRM, and PD after HCT over time across patient subgroups.

Multiple Cox regression models were used for multivariate risk factor analysis for PD, NRM, OS, and PFS after HCT. Clinical factors evaluated in the PD, NRM, OS, and PFS analyses were patient age at the time of HCT (continuous), HCT-CI (0, 1-2, 3 or more), conditioning (CST, RIST), donor (HLA-matched related, HLA-mismatched related or unrelated), disease type (leukemia/MDS, lymphoma), and chemotherapy within 2 months before HCT (yes, no). Logistic regression analysis was performed to identify prognostic factors that were associated with the achievement of CR. In addition to the variables examined in the Cox analysis, blast percentage ($\geq$20%, <20%) in the bone marrow or peripheral blood and the serum lactate dehydrogenase (LDH) level (normal, elevation) before HCT were included for the analysis of CR in patients with leukemia/MDS and those with lymphoma, respectively. We considered 2-sided P-values of <.05 to be statistically significant. Statistical analyses were performed with the SAS version 8.2 (SAS Inc, Cary, NC).

RESULTS

Patient Characteristics

The characteristics of all patients who underwent CST (n = 52) or RIST (n = 80) are summarized in Table 1. The median age of the RIST group was significantly higher than that of the CST group (53 years versus 40 years, $P < .01$). A large number of patients in both groups had acute myeloid leukemia (AML) or MDS (CST 67%, RIST 49%), and the RIST group included a higher population of patients with malignant lymphoma (CST 13%, RIST 40%). All malignant lymphomas (n = 40) were non-Hodgkin's lymphoma, including aggressive (n = 16), highly aggressive (n = 15), and indolent (n = 9) lymphomas. The distribution of lymphoma subtypes was similar between the 2 groups. Disease status at transplantation included primary refractory (n = 42), refractory relapse (n = 65), blastic crisis, or accelerated phase of CML (n = 8) and untreated disease (n = 17). The distribution of disease status and the proportion of patients who received chemotherapy within 2 months before HCT were similar between the 2 groups. The RIST group contained higher proportions of patients with an HCT-CI score of 1 or more (CST 37%, RIST 65%) and those who received G-CSF-mobilized PBSC (CST 40%, RIST 61%) than the CST group.

In the leukemia/MDS patients (n = 89), the median percentage of blasts (82 patients in bone marrow and 7 patients in peripheral blood) in both groups were similar (CST 29%, RIST 30%). In patients with malignant lymphoma, serum LDH was elevated above the upper normal limit in 3 of 7 (43%) in the CST group compared to 23 of 33 (70%) in the RIST group.

Engraftment and GVHD

The clinical course and response are detailed in Table 2. The median duration of follow-up in surviving patients is 1123 days (range: 367-2044 days) in the CST group and 899 days (range: 334-1961 days) in the RIST group. Neutrophil engraftment was observed in 48 patients (92%) and 75 patients (94%), at a median of 17 days and 12 days, respectively. Engraftment was not confirmed in the remaining 9 patients because of death or PD within 28 days after HCT. The incidences of grade II-IV and grade III-IV aGVHD were similar in the CST and RIST groups (50% versus 50% and 23% versus 28%, respectively). The incidences of cGVHD and chronic extensive GVHD were also similar (46% versus 49% and 34% versus 38%, respectively).

Disease Response

The probabilities of achieving CR as the best response were similar after CST and RIST (77% and 64%, respectively) (Table 2). To examine the possible risk factors for achieving CR, we separately analyzed patients with leukemia/MDS and those with lymphoma using a logistic regression analysis (Table 3). Conditioning regimen (RIST) did not influence the CR rate in patients with leukemia/MDS (odds ratio [OR] 1.11, 95% confidence interval [CI] 0.40-3.07,

Table 2. *Clinical Course and Response*

	CST (N = 52)	RIST (N = 80)
Median follow-up of surviving patients, days	1123 (367–2044)	899 (334–1961)
Engraftment of neutrophils, N (%)	48 (92)	75 (94)
Median day (range)	17 (10–35)	12 (5–43)
Acute GVHD, N (%)		
Grade II–IV	26 (50)	40 (50)
Grade III–IV	12 (23)	22 (28)
CR*, N (%)	40 (77)	51 (64)
Leukemia/MDS (n = 89), CR/total	35/45	35/44
Lymphoma (n = 40), CR/total	5/7	14/33
Causes of NRM, N (%)	15 (29)	26 (33)
GVHD	6	11
Infection		
fungus	0	4
CMV	0	1
bacterial	4	7
Interstitial pneumonitis	2	1
Others†	3	2

CST indicates conventional stem cell transplantation; RIST, reduced-intensity stem cell transplantation; GVHD, graft-versus-host disease; MDS, myelodysplastic syndrome; CR, complete remission; NRM, nonrelapse mortality; CMV, cytomegalovirus.

*CR as the best response after transplantation.

†Others included acute myocardial infarction, subarachnoid hemorrhage, and pulmonary alveolar haemorrhage in the CST group, and cerebral hemorrhage and unknown in the RIST group.

P = .84) or in those with lymphoma (OR 0.29, 95% CI 0.05-1.75, P = .18). In the leukemia/MDS patients, those who received chemotherapy within 2 months before HCT (OR 0.32, 95% CI 0.09-1.05, P = .06) and transplant from donors other than an HLA-matched relative (OR 0.28, 95% CI 0.08-1.06, P = .06) tended to have a lower CR rate, whereas the blast percentage (≥20%) of bone marrow or peripheral blood was not associated with the CR rate. In lymphoma patients, chemotherapy within 2 months before HCT was the only factor that was significantly associated with a low CR rate (OR 0.04, 95% CI 0.005-0.40, P < .01), whereas serum LDH elevation did not influence the CR rate.

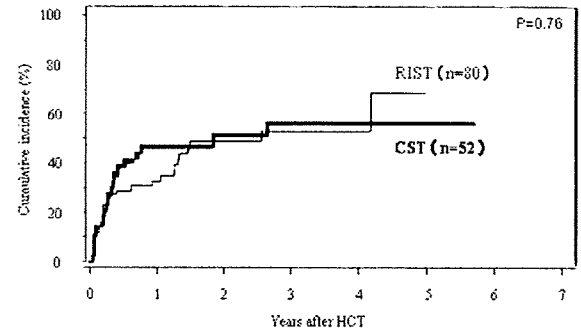

Figure 1. Cumulative incidence of PD. The 2-year probabilities of PD in the CST (51%) and RIST (49%) groups were not significantly different (P = .76).

As shown in Figure 1, the cumulative incidence of PD was not significantly different between the CST and RIST groups. The 2-year probabilities of PD were 51% in the CST group and 49% in the RIST group, which were not significantly different (P = .76). Cox regression analysis was performed to identify factors that were associated with PD. Multivariate analyses in all patients showed that those who received chemotherapy within 2 months before HCT were associated with an increased risk of PD (hazard ratio [HR] 3.93, 95% CI 1.97-7.83, P < .01) (Table 4). After adjusting for these variables, the intensity of conditioning (CST or RIST) did not influence the rate of PD in any of the patients. To further evaluate the association between risk factors and outcome, we performed a subset analysis in patients who underwent CST or RIST. As a result, chemotherapy within 2

Table 3. *Logistic Analysis of CR Rate in Leukemia/MDS and Lymphoma Patients*

		Leukemia/MDS (N = 89)		Lymphoma (N = 40)	
		Odds Ratio (95% CI)	P	Odds Ratio (95% CI)	P
HCT-CI	0	1.00		1.00	
	1–2	1.44 (0.43–4.87)	.56	3.33 (0.66–16.7)	.14
	3 or more	0.96 (0.28–3.35)	.95	2.22 (0.40–12.3)	.36
Age		1.00 (0.97–1.04)	.70	1.02 (0.97–1.07)	.49
Conditioning	RIST	1.11 (0.40–3.07)	.84	0.29 (0.05–1.75)	.18
Donor	Alternative*	0.28 (0.08–1.06)	.06	0.95 (0.26–3.42)	.93
Chemotherapy within 2 months before HCT	Yes	0.32 (0.09–1.05)	.06	0.04 (0.005–0.40)	<.01
Blasts†	≥20%	0.62 (0.21–1.80)	.38		
Serum LDH level	Elevation			0.35 (0.09–1.34)	.12

MDS indicates myelodysplastic syndrome; HCT-CI, hematopoietic cell transplantation-specific comorbidity index; RIST, reduced-intensity stem cell transplantation; LDH, lactate dehydrogenase; CI, confidence interval.

*Non-HLA-matched related donor.

†Blast counts in bone marrow (N = 82) or peripheral blood (N = 7).

Table 4. *Multivariate Analysis of PD, NRM, OS, and PFS in All Patients*

Covariates*	N	PD HR (95% CI)	PD P	NRM HR (95% CI)	NRM P	OS HR (95% CI)	OS P	PFS HR (95% CI)	PFS P
Conditioning									
CST	52	1.00		1.00		1.00		1.00	
RIST	80	0.91 (0.53-1.55)	.72	0.99 (0.51-1.96)	.99	0.95 (0.60-1.51)	.83	0.95 (0.63-1.43)	.79
HCT-CI score									
0	65			1.00		1.00		1.00	
1-2	38			3.25 (1.43-7.40)	<.01	1.76 (1.08-2.89)	.02		
3 or more	29			6.61 (2.88-15.2)	<.01	2.62 (1.51-4.56)	<.01	1.63 (1.02-2.62)	.04
Donor									
MRD	58			1.00		1.00			
Alternative†	74			2.77 (1.39-5.54)	<.01	1.80 (1.15-2.82)	.01		
Chemotherapy within 2 months before HCT									
No	47	1.00				1.00		1.00	
Yes	85	3.93 (1.97-7.83)	<.01			1.73 (1.10-2.72)	.02	2.23 (1.44-3.45)	<.01

PD indicates progressive disease or relapse; NRM, nonrelapse mortality; OS, overall survival; PFS, progression-free survival; HR, hazard ratio; CST, conventional stem cell transplantation; RIST, reduced-intensity stem cell transplantation; HCT-CI, hematopoietic cell transplantation-specific comorbidity index; MRD, HLA-matched related donor; HCT, hematopoietic cell transplantation.

*Factors analyzed included age at the time of HCT (continuous), HCT-CI (0, 1–2, 3, or more), conditioning (CST, RIST), donor (MRD, Alternative), disease type (leukemia/MDS, lymphoma) and chemotherapy within 2 months before HCT (yes, no).

†Non-HLA-matched related donor.

months before HCT was associated with an increased risk of PD only in the RIST group, and not in the CST group (Table 5).

NRM

Major causes of NRM for patients in both groups were GVHD and infection (Table 2). More patients died of fungal infection in the RIST group compared to the CST group, but the 2-year probabilities of NRM were not significantly different (36% and 38%, $P = .50$, Figure 2). A Cox regression analysis was performed to identify factors associated with NRM. Multivariate analyses in all patients showed that a higher HCT-CI score (1 or more) and transplant from an HLA-mismatched related or unrelated donor (alternative donor) were associated with an increased risk of NRM (Table 4). After adjusting for these variables, the intensity of conditioning (CST or RIST) did not influence the rate of NRM in any of the patients. A subset analysis revealed that a higher HCT-CI score (1 or more) was associated with increased NRM in the CST group, but not in the RIST group (Table 5). In contrast, transplant from an alternative donor was associated with increased NRM in the RIST group, but not in the CST group.

Survival

The 2-year probabilities of OS and PFS were not significantly different between the CST and RIST groups (31% and 38%, $P = .98$, for OS; 28% and

Table 5. *Multivariate Analysis of Outcomes after HCT in the CST and RIST Groups*

	Covariates	CST (N = 52) HR (95% CI)	CST (N = 52) P	RIST (N = 80) HR (95% CI)	RIST (N = 80) P
PD	Chemotherapy within 2 months before HCT		NS	6.16 (2.15–17.7)	<.01
NRM	HCT-CI (1–2)	4.48 (1.26–16.0)	.02		NS
	HCT-CI (3 or more)	10.2 (2.91–35.7)	<.01	2.41 (1.14–5.10)	.02
	Alternative donor*		NS	4.63 (1.96–10.9)	<.01
OS	HCT-CI (1–2)	2.69 (1.23–5.90)	.01		NS
	HCT-CI (3 or more)	4.84 (1.97–11.9)	<.01		NS
	Alternative donor*		NS	3.04 (1.73–5.35)	<.01
PFS	HCT-CI (3 or more)	2.26 (1.01–5.04)	.04		NS
	Chemotherapy within 2 months before HCT	2.10 (1.05–4.19)	.03	2.10 (1.19–3.70)	.01
	Alternative donor*		NS	1.79 (1.06–3.00)	.03

PD, indicates progressive disease or relapse; NRM, nonrelapse mortality; OS, overall survival; PFS, progression-free survival; HR, hazard ratio; CST, conventional stem cell transplantation; RIST, reduced-intensity stem cell transplantation; HCT, hematopoietic cell transplantation; HCT-CI, hematopoietic cell transplantation-specific comorbidity index; NS; not significant.

*Non-HLA-matched related donor.

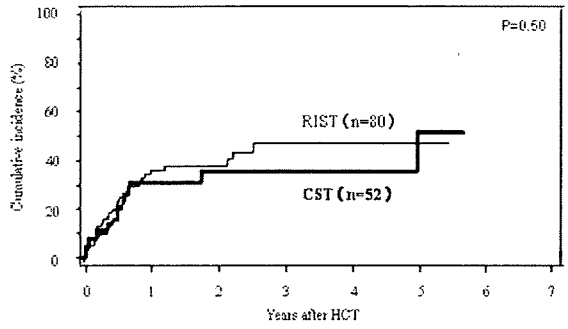

Figure 2. Cumulative incidence of NRM. The 2-year probabilities of NRM in the CST (36%) and RIST (38%) groups were not significantly different (P = .50).

29%, P = .89, for PFS), as shown in Figure 3 and Figure 4. The 2-year probabilities of PD, OS, and PFS were not significantly different between patients who developed grade III-IV aGVHD and those who did not (37% and 44%, P = .39, for PD; 33% and 50%, P = .07, for OS; 27% and 41%, P = .24, for PFS). On the other hand, the 2-year probability of NRM in patients who developed grade III-IV aGVHD was significantly higher than that in those who did not (56% and 21%, P = .004). We also evaluated outcomes in patients who had AML or MDS (CST, n = 35; RIST, n = 39). There was no significant difference in the 2-year probabilities of PD (50% and 51%), OS (37% and 33%), and PFS (34% and 22%) between the CST and RIST groups. On the other hand, the 2-year probability of NRM in the RIST group was significantly higher than that in the CST group (52% and 23%, P = .03).

Multivariate analyses in all patients showed that a higher HCT-CI score (1 or more) and transplant from an alternative donor were associated with poor OS, and patients who received chemotherapy within 2 months before HCT were associated with poor OS and PFS (Table 4). After adjusting for these variables, the risks of OS and PFS were not significantly different between the CST and RIST groups. Disease type (leukemia/MDS or lymphoma) was not a significant factor for OS or PFS. Furthermore, subset analyses revealed that a higher HCT-CI score (1 or more) was associated with poor OS and PFS in the CST group, but not in the RIST group (Table 5). In contrast, transplant from an alternative donor was associated with increased NRM in the RIST group, but not in the CST group. Patients who received chemotherapy within 2 months before HCT had a poor PFS in both groups.

DISCUSSION

Our results suggest that the antileukemia/lymphoma effect of RIST might be comparable to that of CST for hematologic malignancies that are not in remission. We found that a higher HCT-CI score and transplant from an alternative donor were associated with increased risks of NRM and poor OS, and patients who received chemotherapy within 2 months before HCT because of the acceleration of disease progression were associated with increased risks of PD, poor OS, and PFS. The estimated rates of NRM, PD, OS, and PFS in the RIST group were not significantly different from those in the CST group even though the patients who received RIST were significantly older and had significantly higher HCT-CI scores than those who received CST. Several reports have described a similar OS rate in older patients who underwent RIST and CST because the lower NRM rate was offset by a higher PD [5,27,28]. In contrast, Scott et al. [7] found no significant differences in OS, PFS, PD, or NRM between CST and RIST in patients with MDS/AML.

In this study, disease response to the transplantation procedure was similar between the CST and RIST groups when the CR rate is considered the best response, as were the rate and timing of PD. Whereas some reports have shown that PD after HCT was increased in patients who underwent RIST compared to CST [3,5,11], others have found no significant difference [6-8,29]. This discrepancy might result from the differences in disease status at the time of

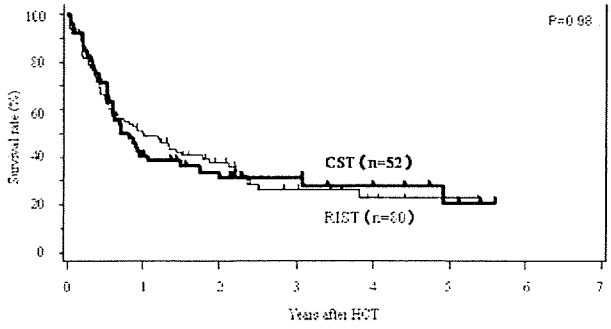

Figure 3. Estimated OS according to the conditioning regimen. The 2-year probabilities of OS in the CST (31%) and RIST (38%) groups were not significantly different (P = .98).

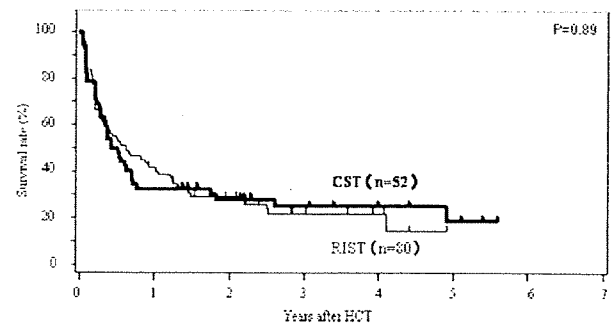

Figure 4. Estimated PFS according to the conditioning regimen. The 2-year probabilities of PFS in the CST (28%) and RIST (29%) groups were not significantly different (P = .89).

transplantation and the intensity of the conditioning regimens. In our study, the median percentage of blasts in leukemia/MDS patients and the distribution of serum LDH levels in lymphoma patients were comparable between the CST and RIST groups. The proportion of patients who required chemotherapy within 2 months before HCT was similar in the 2 groups. Overall, the risk of disease progression was comparable. The lack of a significant difference in PD between the CST and RIST groups in our study may be because the reduced-intensity regimens used in our study were more intense than those in previous reports. Nevertheless, our results suggest that RIST has a comparable antileukemia/lymphoma activity through a GVL effect compared to CST.

Our study found that chemotherapy within 2 months before HCT was the only factor that significantly predicted a lower CR rate in lymphoma patients and tended to be associated with a lower CR rate in leukemia/MDS patients. Furthermore, chemotherapy within 2 months before HCT was also associated with a worse prognosis not only with regard to PD but also for OS and PFS. A subset analysis showed that this negative impact of recent chemotherapy was only seen in RIST patients, and not in CST patients, which suggests that the tempo of the progression of the disease before HCT is especially important in RIST patients. Wong et al. [30] reported that high peripheral blast counts (≥30%) in patients with AML/MDS were associated with poor event-free survival and OS after HCT regardless of the conditioning regimen. In our study, however, ≥20% of blasts in the bone marrow or peripheral blood and serum LDH level elevation did not have a significant impact on the CR rate in leukemia/MDS and lymphoma patients, respectively.

In our study, there was no significant difference in NRM between the CST and RIST groups, which was in contrast to previous reports showing that reduced-intensity regimens were associated with less organ damage, and thus contributed to less NRM [1,4,5,9,27,31-34]. There are several possible explanations for this discrepancy. First, the patients who received RIST were older and had a higher HCT-CI score than those in the CST group. Second, the reduced-intensity conditioning (RIC) we used was more toxic than "truly nonmyeloablative" conditioning. Finally, we tapered immunosuppressive medications rapidly, especially in the RIST group, in an attempt to induce a more potent GVL effect, which resulted in more severe GVHD and subsequent infectious complications. However, our data showed that grade III-IV aGVHD did not contribute to a reduction in the rate of PD or to an overall improvement in survival, which was consistent with a previous report [14], although a high rate of NRM in patients with severe aGVHD may have masked its competing event (ie, PD).

We confirmed that HCT-CI was a significant risk factor for NRM and OS in patients not in remission. HCT-CI has recently been introduced to evaluate pretransplant comorbidities in HCT recipients, which predict well NRM and OS after allogeneic HCT [20]. In this study, the proportion of patients who were not in remission and were associated with comorbidities was 53%, which was higher than the value (42%) in our previous report [21], probably because these patients tended to be heavily pretreated and were forced to pursue HCT in the hope of a rare cure. Interestingly, this negative impact of HCT-CI was only seen in patients who underwent CST, and not in those who underwent RIST. Our data imply that RIC may be preferable in patients with hematologic malignancies not in remission and with a high HCT-CI score by reducing early NRM after transplantation.

Transplant from an alternative donor was another prognostic factor for NRM and OS in this study, which is consistent with previous reports [12,35-38]. Furthermore, an increased risk of NRM and OS associated with alternative donors was observed only in patients who underwent RIST. There are several possible explanations. First, the Japan Marrow Donor Program allows the donation of bone marrow, but not PBSC, from volunteer donors, which has been reported to be associated with poor engraftment and worse outcomes after nonmyeloablative stem cell transplantation [13]. Second, our conditioning regimen including low-dose TBI for RIST from an alternative donor was more toxic than that for RIST from an HLA-matched related donor. Further studies are required to establish optimized conditioning regimens and GVHD prophylaxis for RIST in unrelated pair settings.

In 27 patients who had all of these risk factors (ie, chemotherapy within 2 months beore HCT, HCT-CI score of 1 or more, and transplant from an alternative donor), the 2-year probabilities of NRM, PD, and OS were 56%, 44%, and 21%, respectively, with no significant differences between the CST and RIST groups (data not shown). Therefore, the indications for transplantation in patients with multiple risk factors should be carefully determined.

This study has several inherent limitations. First, the eligibility requirements for CST and RIST were different. Most patients who received RIST were considered ineligible for CST because of age or comorbid conditions. Second, factors other than the conditioning regimen were not entirely comparable between the 2 groups, that is, patient age, underlying diagnosis (leukemia/MDS and lymphoma), donor selection, stem cell source, and GVHD prophylaxis. Third, some of the conventional cytoreductive conditioning regimens we used (ie, use of oral BU and lack of its pharmacologic monitoring) may no longer be considered optimal. Fourth, because the reduced-intensity

regimens used in our study were more intense than those in previous reports, our data may not be generalized to the concept of "reduced-intensity regimen" and there may be circumstances where PD would be more marked. Finally, the follow-up of patients in this study was too short to draw any definite conclusions. Nevertheless, the observed data may still be useful in evaluating the impact of RIST on disease control in patients suffering from a higher risk of disease progression after transplantation.

In conclusion, our results suggest that the antileukemia/lymphoma effect associated with RIST might be comparable to that of CST for hematologic malignancies not in remission, particularly when patients do not require chemotherapy within 2 months before HCT or they had a higher HCT-CI score. To determine the ultimate utility of specific conditioning regimens, controlled prospective trials are needed, with enrolled patients being stratified according to disease activity, hematopoietic stem cell source, and associated comorbidities.

ACKNOWLEDGMENTS

This work was supported in part by grants from the Ministry of Health, Labor and Welfare, Japan. This paper was presented in part as a poster presentation at the 47th Annual Meeting of the American Society of Hematology, Atlanta, GA, December 2005. We thank the medical, nursing, data processing, and laboratory staffs at National Cancer Center Hospital for their important contributions to this study through dedicated care of the patients. We also thank Yukio Kobayashi, Takashi Watanabe, Fusako Ohara, and Kazuaki Yokoyama for their helpful discussions.

REFERENCES

1. McSweeney PA, Niederwieser D, Shizuru JA, et al. Hematopoietic cell transplantation in older patients with hematologic malignancies: replacing high-dose cytotoxic therapy with graft-versus-tumor effects. *Blood.* 2001;97:3390-3400.
2. Bertz H, Potthoff K, Finke J. Allogeneic stem-cell transplantation from related and unrelated donors in older patients with myeloid leukemia. *J Clin Oncol.* 2003;21:1480-1484.
3. Giralt S, Estey E, Albitar M, et al. Engraftment of allogeneic hematopoietic progenitor cells with purine analog-containing chemotherapy: harnessing graft-versus-leukemia without myeloablative therapy. *Blood.* 1997;89:4531-4536.
4. Slavin S, Nagler A, Naparstek E, et al. Nonmyeloablative stem cell transplantation and cell therapy as an alternative to conventional bone marrow transplantation with lethal cytoreduction for the treatment of malignant and nonmalignant hematologic diseases. *Blood.* 1998;91:756-763.
5. Alyea EP, Haesook T, Soiffer RJ, et al. Comparative outcome of nonmyeloablative and myeloablative allogeneic hematopoietic cell transplantation for patients older than 50 years of age. *Blood.* 2005;105:1810-1814.
6. Valcá rcel D, Martino R, Sierra J, et al. Conventional versus reduced-intensity conditioning regimen for allogeneic stem cell transplantation in patients with hematological malignancies. *Eur J Haematol.* 2005;74:144-151.
7. Scott BL, Sandmaier BM, Storer B, et al. Myeloablative vs nonmyeloablative allogeneic transplantation for patients with myelodysplastic syndrome or acute myelogenous leukemia with multilineage dysplasia: a retrospective analysis. *Leukemia.* 2006; 20:128-135.
8. Kojima R, Kami M, Kanda Y, et al. Comparison between reduced intensity and conventional myeloablative allogeneic stem-cell transplantation in patients with hematologic malignancies aged between 50 and 59 years. *Bone Marrow Transplant.* 2005;36:667-674.
9. Mirlcarek M, Martin PJ, Leisenring W, et al. Graft-versus-host disease after nonmyeloablative versus conventional hematopoietic stem cell transplantation. *Blood.* 2003;102:756-762.
10. Nagler A, Slavin S, Varadi G et al. Allogeneic peripheral blood stem cell transplantation using a fludarabine-based low intensity conditioning regimen for malignant lymphoma. *Bone Marrow Transplant.* 2000;25:1021-1028.
11. Michallet M, Bilger K, Garban F, et al. Allogeneic hematopoietic stem-cell transplantation after nonmyeloablative preparative regimens: impact of pretransplantation and posttransplantation factors on outcome. *J Clin Oncol.* 2001;19:3340-3349.
12. Baron F, Storb R, Storer BE, et al. Factors associated with outcomes in allogeneic hematopoietic cell transplantation with nonmyeloablative conditioning after failed myeloablative hematopoietic cell transplantation. *J Clin Oncol.* 2006;24:4150-4157.
13. Maris MB, Niederwiwser D, Sandmaier BM, et al. HLA-matched unrelated donor hematopoietic cell transplantation after nonmyeloablative conditioning for patients with hematologic malignancies. *Blood.* 2003;102:2021-2030.
14. Baron F, Maris MB, Sandmaier BM, et al. Graft-versus-tumor effects after allogeneic hematopoietic cell transplantation with nonmyeloablative conditioning. *J Clin Oncol.* 2005;23:1993-2003.
15. Saito T, Kanda Y, Kami M, et al. Therapeutic potential of a reduced-intensity preparative regimen for allogeneic transplantation with cladribine, busulfan, and antithymocyte globulin against advanced/refractory acute leukemia/lymphoma. *Clin Cancer Res.* 2002;8:1014-1020.
16. Storb R, Deeg HJ, Whitehead J, et al. Methotrexate and cyclosporine compared with cyclosporine alone for prophylaxis of acute graft versus host disease after marrow transplantation for leukemia. *N Engl J Med.* 1986;314:729-735.
17. Kanda Y, Mineishi S, Saito T, et al. Long-term low-dose acyclovir against varicella-zoster virus reactivation after allogeneic hematopoietic stem cell transplantation. *Bone Marrow Transplant.* 2001;28:689-692.
18. Kanda Y, Mineishi S, Saito T, et al. Response-oriented preemptive therapy against cytomegalovirus disease with low-dose ganciclovir: a prospective evaluation. *Transplantation.* 2002;73: 568-572.
19. Junghanss C, Boeckh M, Carter RA, et al. Incidence and outcome of cytomegalovirus infections following nonmyeloablative compared with myeloablative allogeneic stem cell transplantation, a matched control study. *Blood.* 2002;99:1978-1985.
20. Sorror ML, Maris MB, Storner B, et al. Hematopoietic cell transplantation (HCT)-specific comorbidity index: a new tool for risk assessment before allogeneic HCT. *Blood.* 2005;106:2912-2919.

21. Kato R, Fukuda T, Usui E, et al. Hematopoietic cell transplantation-specific comorbidity index to predict non-relapse mortality and survival after allografting. *Blood.* 2005;106:766a.
22. Glucksberg H, Storb R, Fefer A, et al. Clinical manifestations of graft-versus-host disease in human recipients of marrow from HL-A-matched sibling donors. *Transplantation.* 1974;18: 295-304.
23. Przepiorka D, Weisdorf D, Martin P, et al. Consensus conference on acute GVHD grading. *Bone Marrow Transplant.* 1995; 15:825-828.
24. Sullivan KM, Agura E, Anasetti C, et al. Chronic graft-versus-host disease and other late complications of bone marrow transplantation. *Semin Hematol.* 1991;28:250-259.
25. Cheson BD, Horning SJ, Coiffier B, et al. Report of an international workshop to standardize response criteria for non-Hodgkin's lymphoma. *J Clin Oncol.* 1999;17:1244-1253.
26. Kaplan EL, Meier P. Nonparametric estimation from incomplete observations. *J Am Stat Assoc.* 1958;53:457-481.
27. de Lima M, Anagnostopoulos A, Munsell, et al. Nonablative versus reduced-intensity conditioning regimens in the treatment of acute myeloid leukemia and high-risk myelodysplastic syndrome: dose is relevant for long-term disease control after allogeneic hematopoietic stem cell transplantation. *Blood.* 2004; 104:865-872.
28. Martino R, Iacobelli S, de Witte T, et al. Retrospective comparison of reduced-intensity conditioning and conventional high-dose conditioning for allogeneic hematopoietic stem cell transplantation using HLA-identical sibling donors in myelodysplastic syndromes. *Blood.* 2006;108:836-846.
29. Kim DH, Sohn SK, Baek JH, et al. Retrospective multicenter study of allogeneic peripheral blood stem cell transplantation followed by reduced-intensity conditioning or conventional myeloablative regimen. *Acta Haematol.* 2005;113:220-227.
30. Wong R, Shahjahan M, Wang X, et al. Prognostic factors for outcomes of patients with refractory or relapsed acute myelogenous leukemia or myelodysplastic syndromes undergoing allogeneic progenitor cell transplantation. *Biol Blood Marrow Transplant.* 2005;11:108-114.
31. Fukuda T, Hackman RC, Guthrie KA, et al. Risks and outcomes of idiopathic pneumonia syndrome after non-myeloablative and conventional conditioning regimens for allogeneic hematopoietic stem cell transplantation. *Blood.* 2003;102:2777-2785.
32. Sorror ML, Maris MB, Storer B, et al. Comparing morbidity and mortality of HLA-matched unrelated donor hematopoietic cell transplantation after nonmyeloablative and myeloablative conditioning: influence of pretransplant comorbidities. *Blood.* 2004;104:961-968.
33. Canals C, Martino R, Sureda A, et al. Strategies to reduce transplant-related mortality after allogeneic stem cell transplantation in elderly patients: comparison of reduced-intensity conditioning and unmanipulated peripheral blood stem cells vs a myeloablative regimen and CD34+ cell selection. *Exp Hematol.* 2003;31:1039-1043.
34. Diaconescu R, Flowers CR, Storer B, et al. Morbidity and mortality with nonmyeloablative compared to myeloablative conditioning before hematopoietic cell transplantation from HLA matched related donors. *Blood.* 2004;104:1550-1558.
35. Sasazuki T, Juji T, Morishima Y, et al. Effect of matching of class I HLA alleles on clinical outcome after transplantation of hematopoietic stem cells from an unrelated donor. *N Engl J Med.* 1998;339:1177-1185.
36. Junghanss C, Storb R, Maris MB, et al. Impact of unrelated donor status on the incidence and outcome of cytomegalovirus infections after non-myeloablative allogeneic stem cell transplantation. *Br J Haematol.* 2003;123:662-670.
37. Kanda Y, Chiba S, Hirai H, et al. Allogeneic hematopoietic stem cell transplantation from family members other than HLA-identical siblings over the last decade (1991-2000). *Blood.* 2003;102:1541-1547.
38. Arnold R, De Witte T, van Biezen A, et al. Unrelated bone marrow transplantation in patients with myelodysplastic syndromes and secondary acute myeloid leukemia: an EBMT survey. European Blood and Marrow Transplantation Group. *Bone Marrow Transplant.* 1998;21:1213-1216.