A randomized comparison of 4 courses of standard-dose multiagent chemotherapy versus 3 courses of high-dose cytarabine alone in postremission therapy for acute myeloid leukemia in adults: the JALSG AML201 Study

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We conducted a prospective randomized study to assess the optimal postremission therapy for adult acute myeloid leukemia in patients younger than 65 years in the first complete remission. A total of 781 patients in complete remission were randomly assigned to receive consolidation chemotherapy of either 3 courses of high-dose cytarabine (HiDAC, 2 g/m^2 twice daily for 5 days) alone or 4 courses of conventional standard-dose multiagent chemotherapy (CT) established in the previous JALSG AML97 study. Five-year disease-free survival was 43% for the HiDAC group and 39% for the multiagent CT group (P = .724), and 5-year overall survival was 58% and 56%, respectively (P = .954). Among the favorable cytogenetic risk group (n = 218), 5-year disease-free survival was 57% for HiDAC and 39% for multiagent CT (P = .050), and 5-year overall survival was 75% and 66%, respectively (P = .174). In the HiDAC group, the nadir of leukocyte counts was lower, and the duration of leukocyte less than 1.0 × 10^9/L longer, and the frequency of documented infections higher. The present study demonstrated that the multiagent CT regimen is as effective as our HiDAC regimen for consolidation. Our HiDAC regimen resulted in a beneficial effect on disease-free survival only in the favorable cytogenetic leukemia group. This trial was registered at www.umin.ac.jp/ctr/ as #C000000157. (*Blood*. 2011;117(8): 2366-2372)

Introduction

Approximately 70% to 80% of the newly diagnosed younger adult patients with acute myeloid leukemia (AML) achieve complete remission (CR) when treated with an anthracycline, usually daunorubicin (DNR) or idarubicin (IDR), and cytarabine (Ara-C); however, only approximately one-third of these patients remain free of disease for more than 5 years.[1-5] If CR patients are left untreated, almost all of them will relapse and die.[6] Therefore, postremission therapy is indispensable. Postremission therapy is divided into consolidation and maintenance therapy. In the previous studies of Japan Adult Leukemia Study Group (JALSG) for adult AML (AML87, 89, 92, and 95),[1-3,5] we administered 3 courses of consolidation therapy and 6 courses of intensified maintenance therapy. In the AML97 study,[7] we conducted a randomized study to compare the conventional 3-course consolidation and 6-course maintenance therapies with 4 courses of intensive consolidation therapy without maintenance and demonstrated no difference in overall survival (OS) and disease-free survival (DFS). Therefore, the 4 courses of conventional standard-dose multiagent chemotherapy (CT) became the standard regimen in Japan. On the other hand, multiple cycles of high-dose cytarabine (HiDAC) have been commonly used as consolidation therapy in the United States and other countries. However, our national medical insurance system did not allow us to use HiDAC until 2001, and thus we could not use HiDAC in the previous treatment regimens for leukemia. We therefore conducted this prospective, multicenter cooperative

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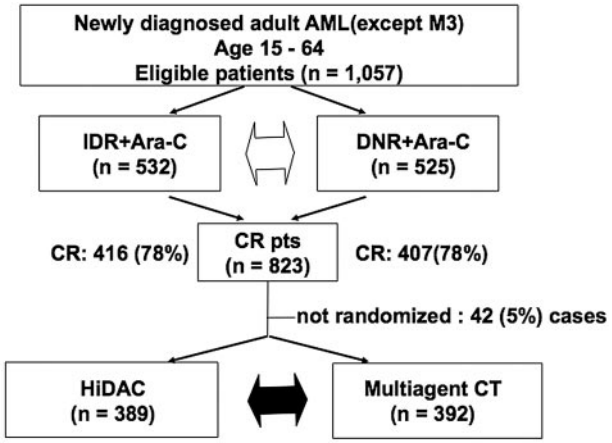

Figure 1. CONSORT diagram.

Table 1. Clinical characteristics of randomized patients

Characteristic	HiDAC (n = 389)	Multiagent CT (n = 392)	P
Age, y, median (range)	46 (15-64)	47 (15-64)	.697
WBC, $\times 10^9$/L, median (range)	15.6 (0.1-382)	14.9 (0.2-260)	.323
Karyotype, n			.210
Favorable	108	110	
Intermediate	242	256	
Adverse	27	14	
Unknown	12	12	
Induction, n			.914
IDR	196	196	
DNR	193	196	
Induction 1 cycle, %	81.0	81.4	.886

study to compare 4 courses of multiagent CT with 3 courses of HiDAC therapy after its approval in April 2001.

Methods

Patients

From December 2001 to December 2005, 1064 newly diagnosed adult patients 15 to 64 years of age with de novo AML were consecutively registered from 129 participating institutions. AML was first diagnosed by the French-American-British classification at each institution. Peripheral blood and bone marrow smears of registered patients were reevaluated by the central review committee. French-American-British M3 was not registered. Eligibility criteria included adequate function of liver (serum bilirubin < 2.0 mg/dL), kidney (serum creatinine < 2.0 mg/dL), heart and lung, and an Eastern Cooperative Oncology Group performance status between 0 and 3. Patients were not eligible if they had prediagnosed myelodysplastic syndrome or prior chemotherapy for other disorders. Cytogenetic abnormalities were grouped by standard criteria and classified according to the Medical Research Council classification.[8] The study was approved by institutional review boards at each participating institution. Written informed consent was obtained from all patients before registration in accordance with the Declaration of Helsinki.

Induction therapy consisted of Ara-C 100 mg/m^2 for 7 days and either IDR (12 mg/m^2 for 3 days) or DNR (50 mg/m^2 for 5 days). If patients did not achieve remission after the first course, the same therapy was administered once more. The outcome of induction therapy was reported to the JALSG Statistical Center before the consolidation therapy started. All CR patients were stratified according to induction regimen, number of courses of induction, age and karyotype, and randomized to receive either 4 courses of multiagent CT or 3 courses of HiDAC therapy. The first course of multiagent CT consisted of mitoxantrone (7 mg/m^2 by 30-minute infusion for 3 days) and Ara-C (200 mg/m^2 by 24-hour continuous infusion for 5 days). The second consisted of DNR (50 mg/m^2 by 30-minute infusion for 3 days) and Ara-C (200 mg/m^2 by 24-hour continuous infusion for 5 days). The third consisted of aclarubicin (20 mg/m^2 by 30-minute infusion for 5 days) and Ara-C (200 mg/m^2 by 24-hour continuous infusion for 5 days). The fourth consisted of Ara-C (200 mg/m^2 by 24-hour continuous infusion for 5 days), etoposide (100 mg/m^2 by 1-hour infusion for 5 days), vincristine (0.8 mg/m^2 by bolus injection on day 8), and vindesine (2 mg/m^2 by bolus injection on day 10). Each consolidation was started as soon as possible after neutrophils, white blood cells (WBCs), and platelets recovered to more than 1.5×10^9/L, 3.0×10^9/L, and 100.0×10^9/L, respectively. In the HiDAC group, 3 courses of Ara-C 2.0 g/m^2 by 3-hour infusion every 12 hours for 5 days were given. Each course was started 1 week after neutrophils, WBCs, and platelets recovered to the aforementioned counts.

Bone marrow examination was performed to confirm CR in both groups before each consolidation therapy and at the end of all consolidation therapy.

Best supportive care, including administration of antibiotics and platelet transfusions, was given if indicated. When patients had life-threatening documented infections during neutropenia, the use of granulocyte colony-stimulating factor was permitted.

After the completion of consolidation therapy, patients received no further chemotherapy. Allogeneic stem cell transplantation (allo-SCT) was offered during the first CR to patients of age 50 years or less with a histocompatible donor in the intermediate or adverse cytogenetic risk groups. Stem cell source was related donor or unrelated donor. Cord blood was not used. Conditioning before transplantation and prophylaxis for graft-versus-host disease were performed according to each institutional standard.

Responses were evaluated by the recommendations of the International Working Group.[9] CR was defined as the presence of all of the following: less than 5% of blasts in bone marrow, no leukemic blasts in peripheral blood, recovery of peripheral neutrophil counts more than 1.0×10^9/L and platelet counts more than 100.0×10^9/L, and no evidence of extramedullary leukemia. Relapse was defined as the presence of at least one of the

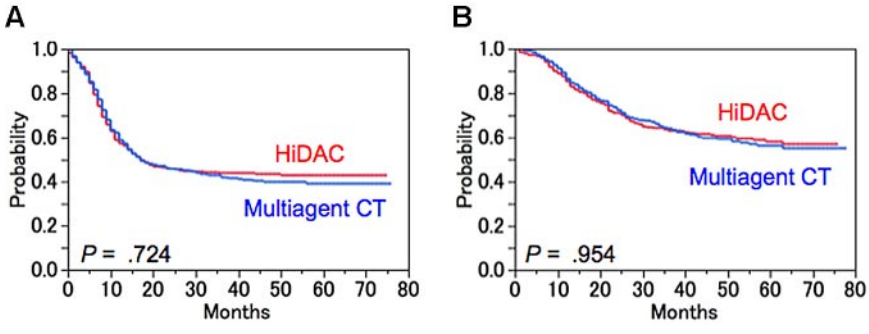

Figure 2. DFS and OS according to treatment arm. (A) DFS of CR patients. Predicted 5-year DFS was 43% for the HiDAC group (n = 389; red line) and 39% for the multiagent CT group (n = 392; blue line; $P = .724$). (B) OS of CR patients. Predicted 5-year OS was 58% for the HiDAC group (n = 389; red line) and 56% for the multiagent CT group (n = 392; blue line; $P = .954$).

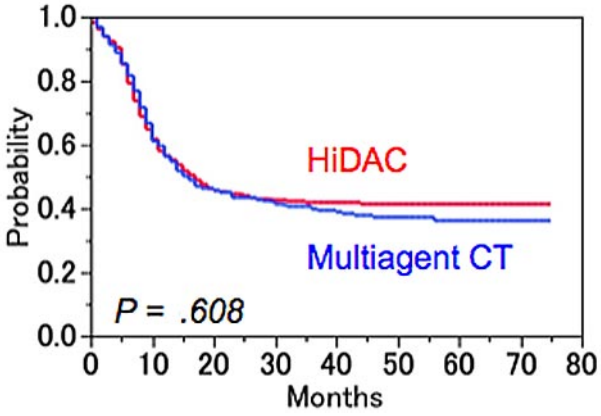

Figure 3. DFS according to treatment arm, after censoring the observation in transplanted patients. Predicted 5-year DFS was 41% for the HiDAC group (n = 389; red line) and 36% for the multiagent CT group (n = 392; blue line; $P = .608$).

following: reappearance of leukemic blasts in peripheral blood, recurrence of more than 5% blasts in bone marrow, and appearance of extramedullary leukemia.

Statistical analysis

This was a multi-institutional randomized phase 3 study with a 2 × 2 factorial design. The primary endpoint of the first randomization was CR rate, and a sample size of 420 patients per group was estimated to have a power of 90% at a 1% level of significance to demonstrate noninferiority (assuming 80% CR rate for both groups). For the second randomization (ie, this study), the primary endpoint was DFS, and the secondary end points were OS and adverse events of grade 3 or more by National Cancer Institute Common Toxicity Criteria. A sample size of 280 patients per group was estimated to have a power of 80% at a 5% level of significance to demonstrate 10% superiority in 5-year DFS for the HiDAC arm (40% vs 30%). OS was defined as the time interval from the date of diagnosis to the date of death. DFS for patients who had achieved CR was defined as the time interval from the date of CR to the date of the first event (either relapse or death). Patients who underwent allo-SCT were not censored. The Kaplan-Meier method was used to estimate probabilities of DFS and OS. For comparison of DFS and OS, the log-rank test was used for univariate analysis and the proportional hazard model of Cox for multivariate analysis. Cumulative incidence of relapse and treatment-related mortality were estimated according to the competing risk method and were evaluated with Gray test. The Wilcoxon rank-sum test was used for continuous data, such as age and WBC count, whereas the χ^2 test was used for ordinal data, such as risk group and frequency of allo-SCT. Statistical analyses were conducted using the JMP program (SAS Institute) and R software Version 2.9.1 (www.r-project.org).

Results

Response to induction therapy

Of 1064 patients registered, 1057 patients were evaluable. Seven patients (1 misdiagnosis, 1 infectious complication, 1 without therapy, and 4 withdrawal of consent) were excluded. Median age was 47 years (range, 15-64 years). Cytogenetic studies were performed in 99.2% of registered patients and the results were available in 97%. Of 1057 evaluable patients, 823 (78%) achieved CR (662 of them after the first induction course). CR rate in the IDR and DNR arms was similar (78.2% vs 77.5%). Percentage of patients who reached CR after the first induction course was also similar (64.1% vs 61.1%, $P = .321$). Day to achieve CR was longer in the IDR arm than the DNR arm (33.8 vs 32.4 days, $P = .038$). The detailed result of induction phase of this study is reported in a separate paper.[10]

Postremission randomization

Of 823 patients who achieved CR, 42 did not undergo the second randomization for a variety of reasons, which included residual toxicity from induction therapy (12), allo-SCT (8), death (1), refusal (1), and unknown (20). The remaining 781 patients were randomly assigned to receive either the HiDAC regimen (389) or the multiagent CT regimen (392; Figure 1). Clinical characteristics of 2 treatment groups were well balanced in age, initial WBC count, cytogenetic risk, induction arm, and induction cycle (Table 1).

DFS and OS

The median follow-up period of living patients was 48 months (range, 5-78 months). Five-year DFS was 43% for the HiDAC group and 39% for the multiagent CT group ($P = .724$; Figure 2A). Five-year OS was 58% for the HiDAC group and 56% for the multiagent CT group ($P = .954$; Figure 2B). After censoring the observation on the date of SCT in transplanted patients, 5-year DFS was 41% for the HiDAC group and 36% for the multiagent CT group ($P = .608$; Figure 3).

The cumulative incidences of relapse and treatment-related mortality during CR, respectively, were 49% and 8% for the HiDAC group and 56% and 5% for the multiagent CT group ($P = .294$, $P = .172$; Figure 4A). After censoring the observation in transplanted patients, those were 55% and 4% for the HiDAC group and 61% and 3% for the multiagent CT group ($P = .402$, $P = .409$), respectively (Figure 4B).

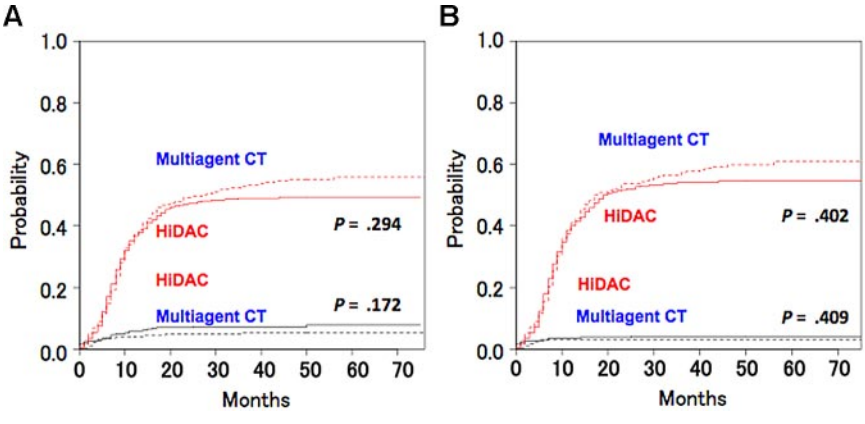

Figure 4. Cumulative incidence of relapse and treatment-related mortality in CR by treatment arm. (A) The incidences of relapse and mortality, respectively, were 49% and 8% for the HiDAC group (solid line) and 56% and 5% for the multiagent CT group (dotted line; $P = .324$, $P = .172$). (B) After censoring the observation in transplanted patients, the incidences of relapse and mortality, respectively, were 55% and 4% for the HiDAC group (solid line) and 61% and 3% for the multiagent CT group (dotted line; $P = .402$, $P = .409$).

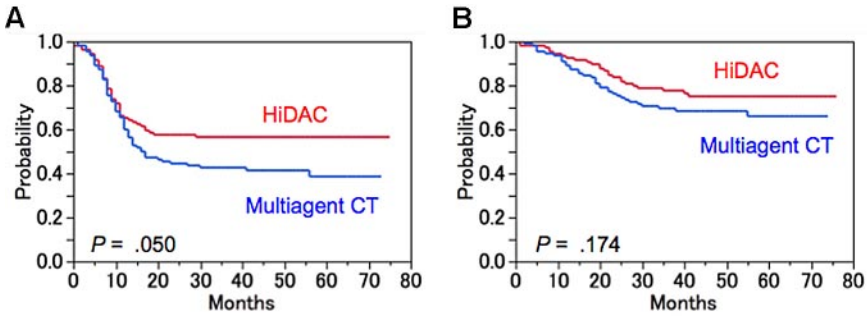

Figure 5. DFS and OS by treatment arm for the favorable cytogenetic risk group. (A) Predicted 5-year DFS was 57% for the HiDAC group (n = 108; red line) and 39% for the multiagent CT group (n = 110; blue line; $P = .050$). (B) Predicted 5-year OS was 75% for the HiDAC group (n = 108; red line) and 66% for the multiagent CT group (n = 110; blue line; $P = .174$).

In patients with the favorable cytogenetics, core-binding factor (CBF) leukemia with t(8;21) or inv(16), 5-year DFS was 57% in the HiDAC group and 39% in the multiagent CT group ($P = .050$; Figure 5A), and 5-year OS was 75% and 66%, respectively ($P = .174$; Figure 5B).

In patients with the intermediate cytogenetics, 5-year DFS was 38% in the HiDAC group and 39% in the multiagent CT group ($P = .403$; Figure 6A), and 5-year OS was 53% and 54%, respectively ($P = .482$; Figure 6B). In patients with the adverse cytogenetics, 5-year DFS was 33% in the HiDAC group and 14% in the multiagent CT group ($P = .364$; Figure 7A), and 5-year OS was 39% and 21%, respectively ($P = .379$; Figure 7B). Among younger patients ($\leq$ 50 years), 5-year DFS was 45% in the HiDAC group and 46% in the multiagent CT group ($P = .590$), and 5-year OS was 62% and 66%, respectively ($P = .228$). Among the older patients ($>$ 50 years), 5-year DFS was 40% in the HiDAC group and 28% in the multiagent CT group ($P = .230$), and 5-year OS was 51% and 40%, respectively ($P = .159$). In patients treated with the IDR regimen at induction, 5-year DFS was 42% in the HiDAC group and 41% in the multiagent CT group ($P = .641$), and 5-year OS was 58% and 57%, respectively ($P = .790$). In patients treated with the DNR regimen at induction, 5-year DFS was 44% in the HiDAC group and 37% in the multiagent CT group ($P = .339$), and 5-year OS was 58% and 56%, respectively ($P = .713$). There was no relationship between the duration of myelosuppression and DFS or OS.

Significant unfavorable prognostic features for DFS by the Cox proportional hazard model were WBC more than 20×10^9/L, the number of induction therapies, and age more than 50 years, and for OS, age more than 50 years, the number of induction therapies, WBC more than 20×10^9/L, and myeloperoxidase-positive blast less than 50%. Induction therapy, consolidation therapy, and cytogenetic risk group were not independent prognostic factors for DFS or OS by this multivariate analysis (Table 2).

Tolerance and toxicity of postremission therapy

All courses of consolidation were administered to 72.5% of patients in the HiDAC group and 70.2% in the multiagent CT group (Table 3). In the HiDAC group, 110 patients (28%) did not receive all 3 courses. The reasons included relapse (18), death in CR (10), allo-SCT (34), adverse events (27), patient's refusal (11), and unknown (10). In the multiagent CT group, 118 patients (30%) did not receive all 4 courses. The reasons included relapse (31), death in CR (8), allo-SCT (42), adverse events (13), patient's refusal (5), and unknown (19). The most common reason was allo-SCT in both groups. Of 125 patients received SCT in first CR, 49 (25 in HiDAC and 24 in multiagent CT) received SCT after completion of full courses of consolidation therapy. The second common reason was adverse events in the HiDAC group and relapse in the multiagent CT group. The patients older than 50 years could tolerate both regimens. Table 4 shows a comparison of both groups regarding the nadir of WBC count and the number of days of WBC less than 1.0×10^9/L. After each course of consolidation, the nadir of WBC count was significantly lower ($P < .0001$) and the day of WBC less than 1.0×10^9/L was significantly longer in the HiDAC group ($P < .001$). During each course of consolidation, the frequency and the number of days of granulocyte colony-stimulating factor administration were significantly higher in the HiDAC group. Table 5 shows toxic adverse events, excluding hematologic side effects. The frequency of documented infections was significantly higher in the HiDAC group ($P < .001$). The subset analysis showed the high incidence of documented infection in HiDAC regimen only in intermediate cytogenetic risk group ($P < .001$).

Discussion

To determine the best postremission therapy, there have been several prospective randomized studies comparing chemotherapy

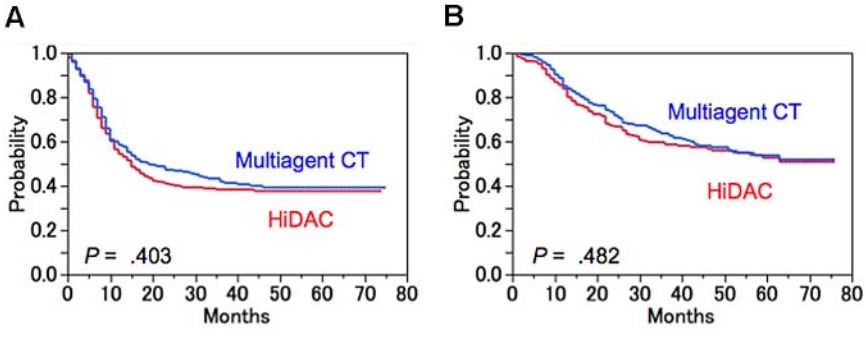

Figure 6. DFS and OS by treatment arm for the intermediate cytogenetic risk group. (A) Predicted 5-year DFS was 38% for the HiDAC group (n = 242; red line) and 39% for the multiagent CT group (n = 256; blue line; $P = .403$). (B) Predicted 5-year OS was 53% for the HiDAC group (n = 242; red line) and 54% for the multiagent CT group (n = 256; blue line; $P = .482$).

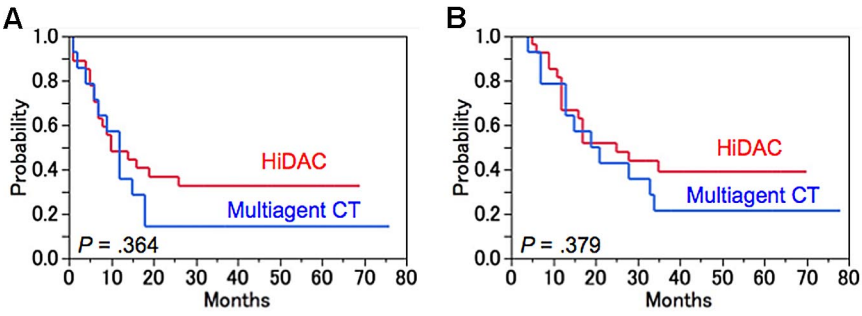

Figure 7. DFS and OS by treatment arm for the adverse cytogenetic risk group. (A) Predicted 5-year DFS was 33% for the HiDAC group (n = 27; red line) and 14% for the multiagent CT group (n = 14; blue line; $P = .364$). (B) Predicted 5-year OS was 39% for the HiDAC group (n = 27; red line) and 21% for the multiagent CT group (n = 14; blue line; $P = .379$).

with SCT. Although there is some limitation in SCT, such as patient age and availability of human leukocyte antigen–identical donors, most randomized studies demonstrate that SCT, the most intensive postremission modality, provides superior or at least noninferior prognosis in high- or intermediate-risk adult AML.[11-13]

As for postremission chemotherapy, HiDAC therapy is generally used in the United States and other countries after the landmark Cancer and Leukemia Group B-8525 (CALGB-8525) study.[14] In Japan, however, because HiDAC therapy was not approved by our national medical insurance system until 2001, combination chemotherapy using non–cross-resistant agents was commonly used in previous studies for adult AML. Therefore, in the current study, we compared conventional multiagent CT with HiDAC therapy.

Our study demonstrated that there is no difference in DFS and OS between the multiagent CT regimen and the HiDAC regimen. The HiDAC regimen, however, was accompanied with more frequent infectious events resulting from more severe and longer-lasting neutropenia. In the CALGB-8525 study,[14] patients randomized to 4 cycles of HiDAC regimen were administered 3 g/m^2 of Ara-C by 3-hour infusion, twice daily on days 1, 3, and 5, and our patients randomized to 3 cycles of HiDAC regimen were given 2 g/m^2 of Ara-C by 3-hour infusion, twice daily for 5 days. Although there were some differences in schedule and dose administered, the total dose of Ara-C was almost the same (72 g/m^2 vs 60 g/m^2). The Acute Leukemia French Association Group compared a timed-sequential consolidation consisting of etoposide, mitoxantrone, and Ara-C with a postremission chemotherapy, including 4 cycles of HiDAC (3 g/m^2), and reported that there were no statistically significant differences between the 2 groups in the rates of event-free survival and OS at 3 years.[15] The British Medical Research Council also compared a conventional Medical Research Council schedule (MACE/MidAC) with 2 courses of HiDAC regimens (3 g/m^2 or 1.5 g/m^2) and reported that there were no significant differences in DFS and OS at 5 years.[16]

On the contrary, the CALGB-8525 study[14] revealed that their HiDAC regimen was superior to the intermediate dose of Ara-C (400 mg/m^2 for 5 days) or to the conventional dose of Ara-C (100 mg/m^2 for 5 days) regimens in DFS and OS; this plausibly comes from the lower dose intensity of the intermediate- or standard-dose Ara-C regimens. Indeed, the CALGB-9222 study[17] showed no difference in DFS and OS between the HiDAC group and the intensified sequential multiagent chemotherapy group.

Cytogenetics is considered one of the most valuable prognostic determinants in adult AML.[8,18] In the present study, although in the intermediate-risk group, the DFS and OS of both consolidation groups were almost identical; in the favorable risk group, the outcome of the HiDAC group (n = 108) tended to be superior to that of the multiagent CT group (n = 110) in DFS (57% vs 39%; $P = .050$) and OS (75% vs 66%; $P = .174$) but not at statistically significant level; and in the adverse risk group, the similar but statistically nonsignificant trend in DFS (33% vs 14%) and OS (39% vs 21%) was noted. Bloomfield et al[19] reported that the HiDAC regimen is the most effective to CBF leukemia. In their study, patients with CBF leukemia (n = 18) had a 78% chance of remaining CR at 5 years when treated with the HiDAC regimen. However, our study showed that DFS of CBF leukemia (n = 108) treated with the HiDAC regimen was only 57% at 5 years.

There are 2 possible explanations of difference between our results and those reported by Bloomfield et al.[19] One is that their superior results may come from a small number of patients (n = 18). Indeed, the CALGB-9222 study,[17] including 28 patients with CBF leukemia, demonstrated that the 5-year DFS and OS of CBF leukemia treated with HiDAC was 60% and 70%, respectively. These data are similar to our results. The other is that CBF leukemia reveals different sensitivity to HiDAC therapy. Some patients with CBF abnormality have KIT mutations, which confer

Table 2. Factors to predict unfavorable prognostic features for DFS and OS by multivariate analysis

Survival type/variable	Category	Hazard ratio	*P*
DFS			
Initial WBC count	≥ 20 × 10^9/L	1.49	< .0001
No. of induction therapies	2 courses	1.50	.0006
Age, y	> 50	1.33	.0028
Consolidation therapy	Multiagent CT	1.04	.7128
OS			
Age, y	> 50	2.00	< .0001
No. of induction therapies	2 courses	1.58	.0033
Initial WBC count	≥ 20 × 10^9/L	1.41	.0070
MPO-positive blast	< 50 %	1.42	.0149
Consolidation therapy	Multiagent CT	0.96	.7768

MPO indicates myeloperoxidase.

Table 3. Tolerance of consolidation

	% receiving the full courses	
	HiDAC	Multiagent CT
All patients	72.5	70.2
Patients ≤ 50 y	71.9	69.0
Patients > 50 y	73.4	71.9
Reason for not receiving the full courses (no. of patients)		
Relapse	18	31
Death	10	8
SCT in first CR	31	42
Adverse event*	27	13
Patient refusal	11	5
Unknown	10	19

*$P < .05$.

Table 4. Intensity of consolidation

	HiDAC	Multiagent CT	*P*
After first consolidation			
Lowest WBC, $\times 10^9$/L	0.17	0.40	< .0001
Days WBC < 1.0 × 10^9/L	13 (0-40)	12 (0-36)	.0005
After second consolidation			
Lowest WBC, $\times 10^9$/L	0.10	0.40	< .0001
Days WBC < 1.0 × 10^9/L	14 (0-34)	13 (0-241)	.0007
After third consolidation			
Lowest WBC, $\times 10^9$/L	0.10	0.40	< .0001
Days WBC < 1.0 × 10^9/L	14 (0-38)	11.5 (0-28)	< .0001
After fourth consolidation			
Lowest WBC, $\times 10^9$/L		0.40	
Days WBC < 1.0 × 10^9/L		12 (0-34)	

Values are median (range).

higher relapse risk on CBF AML.[20,21] CALGB reported that 29.5% of patients with inv(16) and 22% of patients with t(8;21) had KIT mutations, and the cumulative incidence of relapse was higher for patients with mutated KIT than for those with wild-type KIT.[20] The difference of mutation rates of KIT might result in the difference in DFS. Unfortunately, in our present study, KIT mutations were not prospectively evaluated. However, a high mutation rate of KIT is reported among Asian patients with t(8;21) from Japan (37.8%)[22] and China (48.1%).[23] Consequently, JALSG is prospectively evaluating KIT mutation and its impact on the outcome in patients with CBF leukemia treated with repetitive HiDAC therapy. In the adverse cytogenetic risk group, the outcome of the HiDAC group also tends to be better than that of the multiagent CT group, but the difference is not statistically significant. The small number of this cohort may explain the statistical insignificance. Nevertheless, HiDAC therapy may be recommended to this group if patients have no human leukocyte antigen–matched donor.

Recently, IDR is frequently included into induction regimen for AML because of its better effectiveness compared with DNR.[24-26] A meta-analysis of randomized trials showed that the use of IDR instead of DNR results in a high CR rate.[27] However, a German group reported that the advantage of IDR in response rate may be lost during HiDAC consolidation therapy because of increased toxicity in the IDR group.[28] However, our current study demonstrated that, among the HiDAC group, there is no difference in DFS and OS between patients receiving IDR or DNR in induction phase. In our study, although one or 2 courses of the IDR regimen were given before the HiDAC consolidation, only 19% of patients required 2 courses to obtain CR. In contrast, the German group gave 2 courses of IDR induction regimen before the HiDAC consolidation. Thus, severe adverse events during HiDAC therapy probably depend on the total dose of prior IDR. Nevertheless, the HiDAC regimen could be given safely in our patients who had received IDR as induction therapy.

Table 5. Adverse events (CTC grades 3 and 4) during consolidation therapy

	HiDAC, %	Multiagent CT, %	*P*
Documented infection	20.9	14.5	< .001
Febrile neutropenia	66.5	66.4	.311
Bleeding	0.8	0.7	.601
Early death*	0.9	0.6	.389

*Death within 30 days after consolidation chemotherapy.

In conclusion, postremission consolidation regimen should be selected on the basis of prognostic factors, such as cytogenetics. Although several types of HiDAC regimen have been widely adopted as the optimal postremission therapy, the conventional multiagent CT may be recommendable for the intermediate or adverse cytogenetic risk groups. However, our HiDAC regimen should be recommended to the favorable cytogenetic risk group.

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Authorship

Contribution: S.M. designed and performed research, interpreted data, and wrote the manuscript; S.O. designed and performed research, collected and analyzed data, and participated in writing the manuscript; S.F., H.K., K.S., N.U., T.S., K.M., C.N., Y.M., M. Taniwaki, T. Nagai, T.Y., A.F., M. Takahashi, F.Y., Y.K., N.A., H.S., H.H., S.H., K.O., and T. Naoe performed research; and R.O. interpreted data and participated in writing manuscript.

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