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Outcomes in Patients With Relapsed or Refractory Acute Promyelocytic Leukemia Treated With or Without Autologous or Allogeneic Hematopoietic Stem Cell Transplantation

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Abstract

Outcomes in patients with acute promyelocytic leukemia have improved; however, a subset of patients relapse despite receiving all-*trans*-retinoic acid and/or arsenic-based therapies. Among 40 patients with acute promyelocytic leukemia who were treated at our institution (1980–2010), 24 received hematopoietic stem cell transplantation (HCT) (autologous HCT, 7; allogeneic HCT, 14; both, 3); 16 received chemotherapy only. All 3 strategies (autologous HCT, allogeneic HCT, chemotherapy) were feasible in patients with relapsed acute promyelocytic leukemia and result in long-term disease control in selected patients.

Background—Outcomes in patients with acute promyelocytic leukemia (APL) have improved; however, a significant number of patients still relapse despite receiving all-*trans*-retinoic acid (ATRA) and arsenic-based therapies.

Patients and Methods—Outcomes of patients with relapsed APL who were treated at our institution (1980–2010) and who received HCT were compared with those who received chemotherapy (CT) only.

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Disclosure

F. Ravandi has received honoraria from Cephalon and Teva. J. Cortes is a consultant for Teva. The remaining authors have stated that they have no conflicts of interest.

Results—Among 40 patients, 24 received HCT (autologous [auto] HCT, 7; allogeneic [allo] HCT, 14; both, 3); 16 received CT only. The median age at diagnosis was 36 years (range, 13–50 years), 31 years (range, 16–58 years), and 44 years (range, 24–79 years) for the auto-HCT, allo-HCT, and CT groups, respectively. Ten (100%) patients who received auto-HCT and 12 (71%) who received allo-HCT were in complete remission at the time of the HCT. The median follow-ups in the auto-HCT, allo-HCT, and CT groups were 74 months (range, 26–135 months), 118 months (range, 28–284 months), and 122 months (range, 32–216 months), respectively. Transplantation-related mortality (1 year) after auto-HCT and allo-HCT were 10% and 29%, respectively. The 7-year event-free survival after auto-HCT and allo-HCT was 68.6% and 40.6%, respectively ($P = .45$). The 7-year overall survival was 85.7%, 49.4%, and 40% in the auto-HCT, allo-HCT, and CT groups, respectively ($P = .48$).

Conclusion—Both auto-HCT and allo-HCT are associated with durable remission and prolonged survival. All 3 strategies (auto-HCT, allo-HCT, CT) were found to be feasible in the relapsed APL setting and result in long-term disease control in selected patients. In this retrospective analysis, overall survival for patients who received HCT was not significantly better than patients who received CT only, but a trend toward better outcomes was seen in patients who underwent auto-HCT, although not statistically significant.

Keywords

Acute myeloid leukemia; Acute promyelocytic leukemia; Allogeneic transplantation; Autologous transplantation; Bone marrow transplantation; Stem cell transplantation

Introduction

Over the past 20 years, advances in the treatment for newly diagnosed acute APL that included all-*trans*-retinoic acid (ATRA) have yielded high complete remission (CR) rates, which approached 90% or higher.^{1–3} Analysis of recent data also suggests the role of arsenic trioxide (ATO) as part of frontline APL regimens.^{4–8} Despite optimal therapy, relapses still occur in 15% to 25% of the cases.^{9–11} The approach to relapsed or refractory APL is less clearly defined. Most patients who have relapsed can achieve a second CR with ATRA, ATO, chemotherapy (CT), or a combination of these agents.^{12–25} Autologous (auto) hematopoietic stem cell transplantation (HCT) is one of the therapeutic options for consolidation in patients who achieve a second CR and are in molecular remission (MR).^{16–18} Allogeneic (allo) HCT offers a lower relapse risk than auto-HCT, but many patients are not eligible due to comorbidities or the lack of a suitable donor, and allo-HCT is associated with higher transplantation-related morbidity and with transplantation-related mortality [TRM]).^{19–21}

In the largest study to date by Sanz et al,²¹ the investigators retrospectively analyzed outcomes in 625 patients with APL who were treated as part of the European Cooperative Group for Blood and Marrow Transplantation and who underwent either an auto- or allo-HCT. In this study, similar outcomes were shown for both auto- and allo-HCT, although the allo-HCT had a higher incidence of nonrelapse mortality, whereas the auto-HCT group had a higher risk of relapse. This study included patients who were in first complete remission (CR1) or second complete remission (CR2) and found that, even in the ATRA era, there was

utility for HCT, especially for patients who achieved CR2. The purpose of this study was to retrospectively analyze and compare the outcome of patients with relapsed and/or refractory APL who were treated with an auto-HCT, allo-HCT, or CT alone at The University of Texas MD Anderson Cancer Center (MDACC).

Patients and Methods

Patients

We reviewed the records from the Department of Leukemia and the Department of Stem Cell Transplantation at MDACC for patients with relapsed or refractory APL who were treated from January 1980 through December 2010. This study was approved by the institutional review board at our institution (DR10-0651). The diagnosis of relapsed APL was confirmed with a bone marrow aspirate and/or biopsy, and with cytogenetics for translocation t(15;17) or real-time polymerase chain reaction (PCR) for the promyelocytic locus gene (PML)-retinoic acid receptor alpha (RARA) fusion transcript. Real-time PCR analysis was performed on bone marrow cells by using a previously described PCR technique for PML-RARA amplification.^{22,23}

Response Definitions

CR was defined based on the criteria reported by the International Working Group²⁴: an absolute neutrophil count more than 1000 k/ μ L, platelet count higher than 100,000 k/ μ L, transfusion independence, and less than 5% blasts in bone marrow. Relapse was defined as more than 5% blasts in the bone marrow. MR and molecular relapse were defined as the absence or the presence of the PML-RARA fusion transcript by using real-time PCR. For patients who received an HCT, the day of engraftment was defined as the first of the 3 consecutive days with an absolute neutrophil count of 500 k/ μ L.

Infectious Disease and Graft-vs-host Disease Prophylaxis

Infectious disease prophylaxis followed general guidelines from the Department of Stem Cell Transplantation at our institution. Most of the patients received a quinolone for antibacterial prophylaxis, valacyclovir and/or valganciclovir for antiviral and/or cytomegalovirus prophylaxis, sulfamethoxazole and trimethoprim for *Pneumocystis jiroveci* prophylaxis and fluconazole and/or voriconazole for antifungal prophylaxis. Graft-vs-host disease (GVHD) prophylaxis consisted of tacrolimus¹ and mycophenolate in 9 patients, cyclosporine with or with methotrexate with or without corticosteroids in 6, tacrolimus, mycophenolate, and cyclosporine in 1 patient, and tacrolimus and mycophenolate in 1 patient.

Outcomes

The following outcome measures were evaluated: relapse, event-free-survival (EFS) after auto- or allo-HCT, overall survival (OS), treatment-related mortality, acute and chronic GVHD after allo-HCT, and the cause of death. The OS was calculated from the time of diagnosis to the date of the last follow-up or death due to any cause. EFS was calculated from the time of auto- or allo-HCT to the date of relapse, last follow-up, or death due to any cause. For the purposes of reporting EFS and OS for this analysis, the patients who received

both an auto-HCT and an allo-HCT (n = 3) were grouped under allo-HCT because this was the last transplantation that these 3 patients had received.

Statistical Analysis

Patient demographic and clinical characteristics were summarized by using descriptive statistics such as mean (SD), median, inter-quartile range, frequency when appropriate. The Student *t* test, Wilcoxon test, and Kruskal-Wallis test, and/or analysis of variance were used to compare continuous variables among different patient groups. The χ^2 test or the Fisher exact test was applied to assess the association between 2 categorical variables.²⁵ The distributions of EFS and OS were estimated by the Kaplan-Meier method. The log-rank test was performed to test the difference in survival among the groups.²⁶ SAS version 9.1 (SAS Institute Inc, Cary, NC) and S-Plus version 8.0 (Insightful Corporation, Seattle, WA) were used to carry out the computations for all analyses.

Results

Patient Characteristics

A total of 40 patients with relapsed APL were identified: 7 received an auto-HCT, 14 received an allo-HCT, and 3 received both auto- and allo-HCT (first an auto- and later an allo-HCT for relapse in all 3 of these patients), and 16 received CT only. Twelve allo-HCTs were from a matched related donor, whereas 5 were from a matched unrelated donor. Patient characteristics are summarized in Table 1. Five patients had a history of a malignancy: 2 patients in the allo-HCT group (breast cancer, 1; cervical cancer, 1) and 3 patients in the CT group (cervical cancer, 1; sarcoma, 1; squamous cell cancer of head and neck, 1). One patient in the auto-HCT group had received a liver transplantation for primary biliary cirrhosis 1 year before the APL diagnosis. This patient went on to receive auto-HCT while in fourth complete remission (CR4) nine years after the APL diagnosis. Ten (100%) patients who received an auto-HCT and 12 (71%) patients who received an allo-HCT achieved CR before transplantation.

In the auto-HCT group, at the time of HCT, 7 patients were in CR2, 2 patients were in third complete remission (CR3), and 1 patient was in CR4. In the allo-HCT group at the time of HCT, 1 patient was in CR1, 5 patients were in CR2, 6 patients were in CR3, 2 patients were in first relapse, 2 patients were in second relapse, and 1 patient was in third relapse with unknown remission status at the time of HCT. Real-time PCR testing revealed that 7 of 7 patients evaluable for auto-HCT and 5 of 7 patients evaluable for allo-HCT were in MR at the time of HCT (Table 2).

Thirty-five (88%) of 40 patients received some formulation of ATRA as part of induction CT. Nine (90%) of 10 in the auto-HCT group, 13 (76%) of 17 in the allo-HCT group, and 16 (100%) of 16 of the CT group received ATRA-based induction CT. The 5 patients who did not receive ATRA-based induction therapy were diagnosed in 1994 or earlier, and 2 of these 5 patients went on to receive ATRA as salvage therapy. Fewer patients received ATO-based therapy for induction during the study period: 0 of 7 patients who received auto-HCT, 4 (24%) of 17 patients who received allo-HCT, and 2 (13%) of 16 patients who received CT.

Salvage CT regimens varied during the study period, because there was no widely established standard of treatment for relapsed APL. The reasons that 16 patients did not receive either auto- or allo-HCT, which included death due to relapse, serious comorbidities (eg, cardiomyopathy), or patient preference, are summarized in Table 3. The reasons for undergoing an auto-HCT instead of an allo-HCT were MR after salvage CT, lack of a matched donor, and serious comorbidities.

Auto- and Allo-HCT

The characteristics of patients who received HCT are shown in Table 2. The mean CD34⁺ cells/kg infused were 4.67 CD34⁺ cells/kg (range, 1.54–6.81 CD34⁺ cells/kg) and 4.3 CD34⁺ cells/kg (range, 1.77–6.94 CD34⁺ cells/kg) in the patients who received auto-HCT and allo-HCT, respectively. In the auto-HCT group, the conditioning regimens were: busulfan (Bu)¹ (0.8 mg/kg every 6 hours for 4 days) plus cyclophosphamide (Cy) (60 mg/kg for 2 days) in 5 patients; Bu (130 mg/m² daily for 4 days) for fludarabine (Flu) (40 mg/m² for 4 days) in 2 patients; thiotepea (200 mg/m² for 3 days) plus Bu (4 mg/kg for 3 days) plus Cy (60 mg/kg for 2 days) in 2 patients; and etoposide plus Cy in 1 patient. In the allo-HCT group, the conditioning regimens were: Bu (0.8 mg/kg × 6 hours for 4 days) plus Cy (60 mg/kg for 2 days) in 3 patients; Flu (40 mg/m² for 4 days) plus Bu (130 mg/m² for 4 days) in 4 patients, thiotepea (250 mg/m² for 3 days) plus Bu (4 mg/kg for 3 days) plus Cy (60 mg/kg for 2 days) in 4 patients; Flu (30 mg/m² for 4 days) plus melphalan¹ (140 mg/m² × 1) with or without antithymocyte globulin (0.5 mg/kg for 2 days) in 3 patients; and total body irradiation based in 3 patients.

Adverse Events and GVHD

Seven (41%) of 17 patients who received an allo-HCT developed acute GVHD: grade 3 (n = 3), grade 2 (n = 3), and grade 1 (n = 1). Eleven (65%) developed chronic GVHD; 4 had limited disease, and 7 had extensive disease. Other commonly experienced transplantation-related toxicities for the HCT cohort included infections (n = 14), mucositis (n = 8), hematuria and/or hemorrhagic cystitis (n = 3), liver toxicity (n = 3), pulmonary and/or alveolar hemorrhage (n = 2), seizures (n = 2), volume overload (n = 2), rash (n = 2), seizures (n = 2), and renal failure (n = 1).

Outcomes

Initial engraftment occurred in 21 (88%) or 24 patients. Two of the 3 patients who did not experience initial engraftment later were engrafted with a second HCT: 1 patient from the auto-HCT group and 1 patient from allo-HCT group. The third patient died of infection and never ultimately engrafted. With regard to the 2 patients who later engrafted on second HCT, 1 patient received a second auto-HCT (from bone marrow harvest instead of peripheral blood) and the second patient received a second allo-HCT (matched unrelated donor).

The median follow-up for surviving patients in the auto-HCT, allo-HCT, and CT groups was 74 months (range, 26–135 months), 118 months (range, 28–284 months), and 122 months (range, 32–216 months), respectively. Three (30%) of 10 patients who received an auto-HCT relapsed with APL. All 3 patients received an allo-HCT later in their treatment course

and were included in the allo-HCT group for this analysis. Among the 17 patients who received an allo-HCT, 3 (18%) eventually relapsed. Fourteen (58%) of the 24 patients who had received either an auto- or an allo-HCT and 7 (44%) of the 16 who received CT were alive at the time of their last follow-up. The 7-year OS was 85.7%, 49.4%, and 40% in the auto-HCT, allo-HCT, and CT groups, respectively, ($P = .48$) (Figure 1). The 7-year EFS after auto-HCT and allo-HCT was 68.6% and 40.6%, respectively ($P = .45$) (Figure 2). Because there were 3 patients who received both auto-HCT and allo-HCT during their treatment course, we also calculated OS curves (Figure 3) and EFS curves (Figure 4) with these 3 patients who were included in the auto-HCT group, with no significant differences noted among the groups in terms of either EFS or OS.

To further analyze the groups, we then focused on those patients who achieved CR status at the time of transplantation. Twelve CRs were noted among 17 patients who had an allo-HCT, and 6 CRs were noted among 7 patients who had an auto-HCT. Kaplan-Meier curves for EFS are shown in Figure 5 (EFS for patients in CR at the time of transplantation with the 3 patients with both auto-HCT and allo-HCT grouped in the allo-HCT group are shown in Figure 5A; and EFS for patients in CR at the time of transplantation with the 3 patients with both auto-HCT and allo-HCT grouped in the auto-HCT group are shown in Figure 5B). These same groups are depicted in terms of OS in Figure 6A and B. No significant difference is noted among these groups.

Because of the heterogeneous nature of data in this retrospective review, we also analyzed outcomes only for those patients who achieved CR2 status. Kaplan-Meier curves for OS for auto-HCT vs. allo-HCT groups for patients in CR2 (Figure 7A) and EFS for auto-HCT, allo-HCT, and CT groups (Figure 7B) for patients in CR2 are shown. Although there was no significant difference among the groups in terms of either EFS or OS, there was a trend toward improved outcomes for the auto-HCT group in terms of EFS.

Ten (42%) of 24 patients who received an HCT and 9 (56%) of 16 patients with CT only had died at the last follow-up. The main causes of death were the following: in the auto-HCT group, infection (2); in the allo-HCT, infection (3), GVHD (3), and relapse (2); and, in the CT group, infection (4), relapse (3), and non-APL and/or non-treatment related (2) (Table 4). TRM after auto-HCT or allo-HCT was 20% (2/10) and 47% (8/17), respectively.

Discussion

The majority of HCTs performed for relapsed and/or refractory APL during our study period were done in patients in second relapse or CR2 and beyond (8 [80%] of 10 of the total auto-HCT and 14 [82%] of 17) allo-HCT, which likely reflects the availability and greater utilization of both ATRA and ATO in induction and first salvage settings, thus effectively delaying use of HCT for many patients with relapsed APL until later salvage settings.

In our study, we found that there was no significant difference in the 7-year relapse-free survival after auto- and allo-HCT (68.6% and 40.6%, respectively; $P = .45$). We also found that there was no significant difference in the 7-year OS, which was 85.7%, 49.4%, and 40% in the auto-HCT, allo-HCT, and CT groups, respectively ($P = .48$), which is in contrast to a

study that focused on patients in CR2 (17) that retrospectively evaluated 122 patients with relapsed APL (received allo-HCT [n = 23] or auto-HCT [n = 50]). The investigators found that OS was significantly better ($P = .04$) in the auto-HCT group vs. the allo-HCT group. However, relapse-free survival and EFS did not differ significantly between these 2 groups, which were similar to our results. As expected, the occurrence of TRM at 1 year was higher with allo-HCT than with auto-HCT (29% [5/17] vs. 10% [1/10]). The higher TRM in the allo-HCT group in our study was consistent with 2 recent large retrospective studies, which also showed higher TRM in patients with relapsed APL who received allo-HCT.^{17,19}

Auto-HCT has been evaluated in several studies, mostly in a retrospective fashion. One prospective study initiated by the cancer and leukemia group B demonstrated the feasibility of auto-HCT in CR2 for patients with APL. The study, however, was open for all acute myeloid leukemia (AML) patients with AML not just restricted to patients with APL. The investigators found that their “2-step” approach to auto-HCT resulted in a 5-year DFS of 67% for patients with APL compared with only 16% for all other patients with AML.¹⁸ A retrospective study of 26 patients with APL who achieved either CR1 or CR2 and who underwent auto-HCT demonstrated that this might be an effective treatment option, especially in high-risk patients with APL.²⁷ In another study, of 37 patients with relapsed APL, 14 patients received auto-HCT. Compared with the 19 patients who received CT alone, the investigators concluded that treatment that involved an auto-HCT resulted in significantly superior results after a remission induction with ATO-based regimens at relapse.²⁸ Analysis of results of a small retrospective study suggested that auto-HCT performed in CR2 for patients with relapsed APL results in the best outcomes if done in MR (PCR for PML-RAR alpha mutation was undetectable) before auto-HCT.²⁹ Results of 1 prospective study in 15 patients with APL suggest using PCR status to help determine auto- vs. allo-HCT, which concluded that, for patients with APL in CR2 and PCR negativity, auto-HCT be considered and that, for patients with PCR positivity, more aggressive regimens be considered, including those regimens based on allo-HCT.²⁷ In our study, 7 (100%) of 7 patients who underwent auto-HCT only as HCT-based therapy were in CR at the time of HCT, and, of these patients, 5 (71%) of 7 were found to be in MR. All but one of these patients was in CR2 or beyond. The 7-year relapse-free survival for the auto-HCT group was 68.6% and the 7-year OS was 85.7%, with a TRM of 10%, which suggests that auto-HCT is indeed an effective treatment in CR2 and beyond for patients with relapsed APL.

There are several limitations of the current analysis. One of the limitations of the present study is indeed its retrospective nature. However, despite a low incidence of relapsed and/or refractory APL cases overall, we were able to identify 40 patients at a single academic medical center. Although there was no standard salvage regimen in APL, especially before the wide availability of ATRA and ATO, the majority of patients analyzed had ultimately received one or both of these agents during their treatment course. Another limitation is the inherent bias involved in selection of patients for auto- or allo-HCT. For example, patients must have adequate organ function, and performance status, and have achieved CR before being considered for HCT. This is especially relevant for auto-HCT. Because auto-HCT has less morbidity in general than allo-HCT, these patients were likely to demonstrate better

outcomes. In this analysis, the patients with disease refractory to salvage CT either died of complications of relapsed APL (3 patients in the CT group only) or proceeded to allo-HCT while in demonstrable relapse (4 patients in the allo-HCT group). In addition, the allo-HCT group comprised more patients with multiply relapsed APL (53% CR2 or higher vs. 30% in the auto-HCT group), which further demonstrates inherent selection bias.

Conclusion

In this retrospective study, both auto- and allo-HCT are associated with durable remission and prolonged survival. Indeed, we demonstrated that all 3 treatment approaches (auto-HCT, allo-HCT, and CT only) resulted in a proportion of patients who achieved long-term disease control. Although there was no statistically significant difference in the OS of patients who received HCT compared with patients who received CT only, the best outcomes were seen in patients who underwent auto-HCT. Because a number of patients relapsed after HCT, additional treatment issues should be further studied in this setting, including the optimal sequence of auto- and allo-HCT, and the role of maintenance therapy (eg, ATRA- or ATO-based therapy) after HCT. In addition, patients who are deemed ineligible for HCT may be successfully treated with salvage CT only in a few selected patient cases. Given the limitation of a retrospective study, a prospective randomized clinical trial is warranted to identify the best treatment approach for relapsed or refractory APL.

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Clinical Practice Points

- Therapeutic advances in the treatment of APL (including ATRA, ATO, better supportive care) have dramatically improved outcomes and/or cure rates over the past decade. Despite these remarkable improvements, patients with APL are still at risk for morbidity and/or mortality during induction (eg, disseminated intravascular coagulation), and a small subset of patients ultimately relapses.
- Modalities for therapy in the salvage setting for patients with APL have included clinical trial enrollment, retreatment, or treatment with ATRA, ATO, or both; cytotoxic CT; and auto-or allo-HCT.
- In multiple studies, auto-HCT, allo-HCT, or CT have all been used as feasible treatment options, and treatment with auto-HCT demonstrates a trend toward better outcomes in a subset of patients with relapsed APL.

Figure 1.

OS by Treatment: Auto-HCT, Allo-HCT, and CT Alone Groups

Abbreviations: allo = allogeneic; auto = autologous; CT = chemotherapy; E/N = number of events (E) divided by total number (N) in each group; HCT = hematopoietic stem cell transplantation; OS = overall survival.

Figure 2.

EFS by HCT Type: Auto-HCT vs. Allo-HCT

Abbreviations: allo = allogeneic; auto = autologous; EFS = event-free-survival; E/N = number of events (E) divided by total number (N) in each group; HCT = hematopoietic stem cell transplantation.

Figure 3.

OS by Treatment: Auto-HCT, Allo-HCT, and CT Alone Groups (With the 3 Patients Who Received Both Auto-HCT and Allo-HCT Placed in Auto-HCT Group)

Abbreviations: allo = allogeneic; auto = autologous; CT = chemotherapy; E/N = number of events (E) divided by total number (N) in each group; HCT = hematopoietic stem cell transplantation; OS = overall survival.

Figure 4.

EFS by HCT Type: Auto-HCT vs. Allo-HCT (With the 3 Patients Who Received Both Auto-HCT and Allo-HCT Placed in Auto-HCT Group)

Abbreviations: allo = allogeneic; auto = autologous; CT = chemotherapy; EFS = event-free survival; E/N = number of events (E) divided by total number (N) in each group; HCT = hematopoietic stem cell transplantation.

Figure 5.

(A) EFS for Patients in CR at the Time of Transplantation With the 3 Patients With Both Auto-HCT and Allo-HCT Grouped in the Allo-HCT Group. (B) EFS for Patients in CR at the Time of Transplantation, With the 3 Patients With Both Auto-HCT and Allo-HCT Grouped in the Auto-HCT group

Abbreviations: allo = allogeneic; auto = autologous; CR = complete remission; EFS = event-free survival; E/N = number of events (E) divided by total number (N) in each group; HCT = hematopoietic stem cell transplantation.

Figure 6.

(A) OS for Patients in CR at the Time of Transplantation With the 3 Patients With Both Auto-HCT and Allo-HCT Grouped in the Allo-HCT Group. (B) OS for Patients in CR at the Time of Transplantation With the 3 Patients With Both Auto-HCT and Allo-HCT Grouped in the Auto-HCT Group

Abbreviations: allo = allogeneic; auto = autologous; CR = complete remission; E/N = number of events (E) divided by total number (N) in each group; HCT = hematopoietic stem cell transplantation; OS = overall survival.

Figure 7.

(A) Kaplan-Meier Curves for OS for Auto-HCT vs. Allo-HCT Groups. (B) EFS for Auto-HCT, Allo-HCT, and CT Groups

Abbreviations: allo = allogeneic; auto = autologous; CT = chemotherapy; EFS = event-free survival; E/N = number of events (E) divided by total number (N) in each group; HCT = hematopoietic stem cell transplantation; OS = overall survival.

Table 1

Patient Characteristics

Patient Characteristics	Allo-HCT (17)	Auto-HCT (10)	CT (16)	P Value
Median (range) age at diagnosis, y	31 (16–58)	38 (13–53)	44 (24–79)	.089
Sex, no. (%)				.31
Male patients	9 (53)	8 (80)	11 (69)	
Female patients	8 (47)	2 (10)	5 (31)	
Prior malignancies, CT, and XRT	2	0	3	.70
No. relapses, no. (%) ^a				.42
1	8 (47)	7 (70)	9 (56)	
2	9 (53)	2 (20)	5 (31)	
3	0	1 (10)	2 (13)	
No. salvage CT regimens				NA
Non-ATRA, non-ATO CT	5	2	6	
ATRA	6	1	10	
ATRA, CT	11	9	13	
ATO	3	1	4	
ATRA, ATO	3	3	2	
CT, ATO	1	0	2	
ATRA, ATO, CT	0	0	3	
ATRA, ATO, gemtuzumab	8	3	1	
Gemtuzumab	0	1	0	
Retinobenzoic acid (tamibarotene)	2	1	0	
Auto-HCT	3	NA	NA	

Abbreviations: allo = allogeneic; ATO = arsenic trioxide; ATRA = All-trans retinoic acid; auto = autologous; CT = chemotherapy; HCT = hematopoietic stem cell transplantation; NA = not applicable; XRT = radiation therapy.

^aIn the allo- and auto-HCT groups, before transplantation; in the CT group, total.

Table 2**Reasons Why Patients Did Not Receive HCT**

Reason for no HCT	No. Patients (n = 16)
Unknown	1
Death at relapse (subarachnoid hemorrhage [n = 1], brain stem hemorrhage [n = 1], bacterial sepsis and/or multiorgan failure [n = 1])	3
Comorbidities	
Cardiomyopathy	1
Morbid obesity	1
Age	2
Remission with arsenic trioxide	5
Transferred care, lost in follow-up	2
CNS relapse only	1

Abbreviations: CNS = central nervous system; HCT = hematopoietic stem cell transplantation.

Table 3

Characteristics of Patients Who Received HCT

Characteristics	Auto-HCT (n = 10)	Allo-HCT (n = 17)
Status before transplantation, number		
Complete remission	10	12
Molecular remission	7	5
In relapse	0	4
Unknown	0	1
Donor type, number		
Matched related	NA	12
Matched unrelated		5
Stem cell source *1 (one had both)		
Bone marrow	2	8
Peripheral blood	6	9
Unknown source	2	0
Conditioning regimen		
Bu/Cy	5	3
Flu/Bu	2	4
Thiotepa/Bu/Cy	2	4
Cy/etoposide	1	0
TBI based	0	3
Flu/melphalan	0	3
GVHD prophylaxis		
Tacrolimus/mycophenolate/cyclosporine		1
Tacrolimus/methotrexate	NA	9
Tacrolimus/mycophenolate		1
Cyclosporine± methotrexate ± steroids		6
CD34+ cells (cells/kg)		
Mean (range)	4.67 (1.54–6.81)	5.88 (1.77–6.94)
Unknown quantity	3	5

Abbreviations: allo = allogeneic; auto = autologous; Bu = busulfan; Cy = cyclophosphamide; Flu = fludarabine; GVHD = graft-vs-host disease; HCT = hematopoietic stem cell transplantation; HCT = hematopoietic stem cell transplantation; NA = not applicable; TBI = total body irradiation.

Table 4

Causes of Death in the HCT and CT Groups

	Auto-HCT	Allo-HCT	CT
Relapse and/or refractory disease	0	2	3
Infections and/or sepsis	2	3	4
GVHD	0	3	0
Other transplantation-related complications	0	0	0
Nonleukemia and/or nontransplantation related	0	0	2
Total	2/10 (20%)	8/17 (47%)	9/16 (56%)

Abbreviations: allo = allogeneic; auto = autologous; CT = chemotherapy; GVHD = graft-vs-host disease; HCT = hematopoietic stem cell transplantation.