HIGH PROBABILITY OF LONG-TERM SURVIVAL IN 2-YEAR SURVIVORS OF AUTOLOGOUS HEMATOPOIETIC CELL TRANSPLANTATION FOR ACUTE MYELOID LEUKEMIA IN FIRST OR SECOND COMPLETE REMISSION

Navneet S. Majhail, MD, MS¹,², Ruta Bajorunaite, PhD³,⁴, Hillard M. Lazarus, MD⁵, Zhiwei Wang, MS³,⁴, John P. Klein, PhD³,⁴, Mei-Jie Zhang, PhD³,⁴, and J. Douglas Rizzo, MD, MS³,⁴
¹Center for International Blood and Marrow Transplant Research, Minneapolis, MN
²University of Minnesota, Minneapolis, MN
³Center for International Blood and Marrow Transplant Research, Milwaukee, WI
⁴Medical College of Wisconsin, Milwaukee, WI
⁵University Hospitals Case Medical Center, Cleveland, OH

Abstract

We describe long-term outcomes of autologous hematopoietic-cell transplantation (HCT) for 315 acute myeloid leukemia (AML) patients in first or second complete remission (CR). All patients were in continuous CR for ≥2-years post-HCT. Patients were predominantly transplanted in CR1 (78%) and had good or intermediate cytogenetic risk disease (74%). Median followup of survivors was 106 (range, 24-192) months. Overall survival at 10-years post-HCT was 94% (95% confidence intervals, 89-97%) and 80% (67-91%) for patients receiving HCT in CR1 and CR2, respectively. The cumulative incidence of relapse at 10-years post-HCT was 6% (3-10%) and 10% (3-20%) and that of non-relapse mortality was 5% (2-9%) and 11% (4-21%), respectively. On multivariate analysis, HCT in CR2 (vs. CR1), older age at transplantation and poor cytogenetic risk disease were independent predictors of late mortality and adverse disease-free survival. The use of growth factors to promote engraftment following HCT was the only risk factor for relapse. Relative-mortality of these 2-year survivors was comparable to that of age-, race- and gender-matched normal population. Patients who receive an autologous HCT for AML in CR1 or CR2 and remain in remission for ≥2-years have very favorable long-term survival. Their mortality rates are similar to that of the general population.
Introduction

After attainment of an initial remission, patients with acute myeloid leukemia (AML) can receive consolidation therapy with either chemotherapy or hematopoietic-cell transplantation (HCT) based on various prognostic factors (e.g., age, performance status, and cytogenetics). In general, patients with favorable prognostic features receive consolidation chemotherapy only while those with high-risk disease and an acceptable risk of treatment-related morbidity and mortality are offered allogeneic HCT. Autologous HCT has also been investigated as consolidation therapy for AML and can extend survival in a select subgroup of patients (1-12). Although its role has not been clearly defined, autologous HCT continues to be used in the management of patients with AML. For instance, 3049 autologous HCT for AML were reported to the Center for International Blood and Marrow Transplant Research (CIBMTR) from 2000-2007 (unpublished observation).

Relapse is the most common cause of treatment failure among patients who receive an autologous HCT for AML and predominantly occurs within the first 2-years post-transplant (2-10, 13). Long-term survival and risks for late relapse among patients with AML who survive in remission for 2-years after autologous HCT have not been previously described. We conducted a retrospective cohort study to describe the long-term outcomes of patients receiving an autologous HCT for AML who remain in continuous complete remission (CR) for at least 2-years following transplantation. We also conducted analyses to compare their mortality with that of the general population and to identify patient-, disease-, and transplant-related factors that were predictive of late outcomes.

Methods

Data Sources

Data for this study were obtained from the Center for International Blood and Marrow Transplant Research (CIBMTR), which is a voluntary group of >500 transplant centers worldwide. Participating centers register basic information on all consecutive transplants to a Statistical Center at the Medical College of Wisconsin. Detailed demographic and clinical data are collected on a representative sample of registered patients using a weighted randomization scheme. Compliance is monitored by on-site audits. Patients are followed longitudinally, with yearly follow-up. Computerized checks for errors, physician reviews of submitted data, and on-site audits of participating centers ensure the quality of data. Observational studies conducted by the CIBMTR during the time period of this study were done with a waiver of informed consent and are compliant with HIPAA regulations as determined by the Institutional Review Board and the Privacy Officer of the Medical College of Wisconsin.
Patients

Our study included patients reported to the CIBMTR who had received an autologous HCT for AML in first or second complete remission (CR) between 1990 and 1998 in North America and were in continuous CR for at least 2-years after transplantation.

Patients were selected from the research database if they had received a first transplant for AML in CR1 or CR2 and had achieved or maintained a CR for at least 2-years following transplantation. Patients who died or who had persistent or recurrent malignancy within 2-years of their transplant date were eliminated from the dataset. A completeness index of follow-up data was computed for each team with potentially eligible patients (14). Additionally, the proportion of patients with follow-up less than 2-years and no reported events (relapse or death) was calculated. Some transplant teams follow recipients of autologous transplantation long-term less diligently, particularly beyond 1-year after the procedure. In order to avoid potential bias from teams with incomplete follow-up and, consequently, incomplete ascertainment of events in the late post-transplant period, the final dataset included patients from teams where the number of patients evaluated at 5 years or later was greater than 50% of the patients alive and disease-free at 2 years after HCT. Followup information provided by centers was used for this study.

Nine hundred and fifty-eight patients received a first autologous HCT for AML in CR1 or CR2 in the USA and Canada and were reported to the CIBMTR between 1990 and 1998. Among these, 540 patients were excluded for failure to achieve complete remission after HCT, or for death or relapse or second transplant within the first two years post-transplant. An additional 103 patients were excluded from 21 teams that did not meet the followup reporting criteria specified above. The final study population consisted of 315 patients from 63 transplant centers (Table 1). The median followup of survivors was 106 months (range, 24-192 months). The followup completeness index from the time of HCT, which is the ratio of total observed person-time and the potential person-time of followup in a study (14), was 97% at 5-years, and 80% at 10-years.

End Points

Primary study endpoints were overall survival (OS), disease-free survival (DFS), relapse and non-relapse mortality (NRM). For analyses of OS, failure was death from any cause; surviving patients were censored at the date of last contact. DFS was survival in CR; disease relapse or progression and death from any cause were considered as events and patients surviving without disease were censored at the date of last contact. Relapse was defined as recurrence of AML with death as a competing risk. NRM was defined as mortality not related to disease recurrence and relapse was the competing risk. The two competing risks relapse and NRM make up the DFS event.

Statistical Analyses

Univariate probabilities of OS and DFS were calculated by the Kaplan-Meier estimator; the log-rank test was used for univariate comparisons (15). Probabilities of NRM and relapse were calculated by using cumulative incidence curves to accommodate competing risks. Estimates of standard error for the survival function were calculated by Greenwood’s
formula and 95% confidence intervals (CI) were constructed using log-transformed intervals.

Potential patient-, disease- and treatment related prognostic factors (Table 2) for OS, DFS, relapse and NRM were evaluated in multivariate analyses using Cox proportional-hazards regression (16). Multivariate models were built using a stepwise forward selection with a significance level of 0.05. In each model, the assumption of proportional hazards was tested for each variable using a time-dependent covariate (15). First-order interactions of significant covariates were tested.

We calculated estimates of relative mortality as described by Andersen and Vaeth,(17) taking into account differences among patients with regard to age, gender, race and nationality using population-based standard mortality tables for North America (U.S. and Canada). Relative mortality with respect to a transplant recipient is the relative risk of dying at a given time after transplantation as compared with a person of similar age and gender in the general population. Mortality rates with 95 percent confidence intervals for relative mortality that included 1.0 were not considered to indicate a significant difference from the rates in a normal population. Plots for relative excess mortality and their pointwise 95% confidence intervals were constructed and were based on the kernel smoothed estimates with a bandwidth of 2 years using the Epanechnikov kernel. (18)

All P-values are two-sided. All analyses were carried out using SAS statistical software (SAS Institute Inc., Cary, NC, USA).

RESULTS

Patient, Disease and Treatment Characteristics

Table 1 details the demographic, disease and transplant characteristics of our study cohort. The majority of patients received HCT in CR1 (78%) and had intermediate cytogenetic risk disease (54%). Patients predominantly received a bone marrow graft (72%) and total body irradiation based conditioning regimen (75%). Purged graft was administered to 44% recipients.

Univariate Analyses

Univariate probabilities of OS and DFS and cumulative incidences of relapse and NRM are described by disease status at transplant in Table 3. Overall survival at 10-years after HCT was 94% (95% CI, 89-97%) and 80% (95% CI, 67-91%) for patients transplanted in CR1 and CR2 respectively (Figure 1). The probability of disease-free survival at 10-years for CR1 and CR2 patients was 88% (95% CI, 83-93%) and 79% (95% CI, 66-90%) while the 10-year cumulative incidence of relapse was 6% (95% CI, 3-10%) and 10% (3-20%) and that for non-relapse mortality was 5% (95% CI, 2-9%) and 11% (4-21%) (Figure 2), respectively.

Multivariate Analyses

Results of multivariate analyses for OS, DFS, relapse and NRM are detailed in Table 4. HCT in CR2, older age at transplantation and poor cytogenetic risk disease were
independent predictors of higher late mortality. Compared to age <20 years at the time of HCT, patients receiving HCT at older age had higher risks of overall mortality (relative risk for overall mortality 11.43 (95% CI, 1.37-95.61) for age 20-49 years and 32.44 (95% CI, 3.78-278.4) for age ≥50 years at HCT). Patients with poor risk cytogenetics had a relative risk of overall mortality of 12.43 (95% CI, 1.91-81.00) while patients with intermediate risk cytogenetics had comparable mortality risks to patients with good risk cytogenetics. Patients transplanted in CR2 had 3.81 (95% CI, 1.59-9.12) times higher relative risks of mortality compared to patients receiving a transplant in CR1.

The same factors also predicted adverse DFS (Table 4). The only factor predictive of higher relapse was use of hematopoietic growth factors to promote engraftment following HCT. Karnofsky performance score <90 at transplant increased the risks of late NRM.

Causes of Death and Second Cancers

Twenty-four deaths were reported for our study cohort; among these, relapse was the most common cause of death (N=10). Other causes of death included organ failure (N=4), second cancer (N=3), and other causes (e.g., accidental death, hemorrhage, other cause not specified; N=5). The cause of death could not be ascertained for 2 patients. Among the three patients who died of second cancers, specific cancer types included myelodysplastic syndrome (N=2) and non-small cell lung cancer (N=1).

Six secondary cancers have been reported among 315 patients included in our cohort. These have included myelodysplastic syndrome (N=3), non-small cell lung cancer (N=1), cutaneous melanoma (N=1) and papillary carcinoma of the thyroid gland (N=1).

Relative Mortality

The relative mortality of our study cohort was similar to that of the age-, race- and gender-matched general population starting at 4 years after transplantation (Figure 3).

DISCUSSION

Our study indicates very favorable long term survival for patients with AML in CR1 or CR2 who receive an autologous HCT and survive in remission for 2-years or more post-transplant. Mortality rates of these 2-year survivors are similar to general population mortality rates.

In an analysis from the Bone Marrow Transplant Survivor Study, Bhatia et al have also described long-term mortality after autologous HCT for AML (13). Their study included 158 patients with AML who had received an autologous HCT and survived for 2-years after transplantation. The overall relative mortality of their cohort was higher than that of the general population with a standardized mortality ratio of 6.4 (95% confidence intervals, 4.1-9.3). However, mortality rates declined with time since HCT and were no different that the general population in a subgroup of patients who had survived for more than 10 years after HCT. A more recent study from the Fred Hutchinson Cancer Research Center has also shown that patients receiving autologous HCT for hematologic malignancies who survive in remission for at least 5 years have mortality rates that are higher than the general population.
In contrast, our study shows that patients with AML who receive an autologous HCT in CR1 and CR2 have relative mortality rates similar to that of the general population starting at 4-years after HCT. In comparison to other studies, our analysis only included patients in CR1 and CR2 and the majority of patients included in our cohort had good or intermediate risk cytogenetics. Hence, in contrast to other studies where relapse was the most common cause of late mortality, patients included in our study had a relatively lower probability of late relapse and were able to enjoy survival rates similar to the general population.

Advanced disease stage (CR2 vs. CR1), older age at HCT, and presence of high-risk cytogenetic abnormalities are known adverse prognostic factors for AML and it is not surprising that these factors were associated with higher risks of overall mortality and adverse DFS in our patient cohort. A lower Karnofsky performance status score at transplant, which may be a surrogate for comorbidities and intensity and toxicity of prior therapy, was associated with increased risks of late NRM.

The use of hematopoietic growth factors to promote engraftment was the only factor associated with increased risks of relapse. This observation is intriguing and has been reported previously among autologous HCT recipients for lymphoma (20, 21). In a recent retrospective cohort study from the European Group for Blood and Marrow Transplantation, Gorin et al have also reported a higher incidence of relapse with peripheral blood versus bone marrow transplantation among 2,165 AML patients receiving autologous HCT in CR1 (22). The cumulative incidence of relapse was 56%, 46% and 39% among early peripheral blood (≤80 days of CR1), delayed peripheral blood (>80 days from CR1) and bone marrow graft recipients, respectively (P<0.001). These higher risks for relapse with peripheral blood transplantation persisted even after adjusting for other important risk factors in multivariate analyses. The authors postulated that recruitment of tumor cells following mobilization with growth factors with subsequent higher leukemic contamination of the peripheral blood grafts may have accounted for this higher incidence of relapse. The impact of growth factors on outcomes of allogeneic transplantation for leukemia is also controversial, with some studies associating their use with inferior overall and leukemia-free survival while the majority of studies show no impact on outcomes.(23-27) In our study, the adverse effect of growth factors on relapse could be secondary to patient selection factors that we could not account for in our analysis. For instance, our cohort consisted of patients who received their transplant in the 1990’s when the use of growth factors in HCT was emerging and patients at higher risk of relapse may have received growth factors preferentially (e.g. among patients who had received greater prior therapy to achieve CR and may have been considered to be at higher risk of delayed engraftment). However, this observation may warrant further investigation in future studies.

It is reassuring that the mortality rates of AML patients who receive an autologous HCT and stay in remission for 2-years are similar to that of the general population. However, late effects of transplantation such as second cancers and other organ specific late complications can take many years to develop and studies that include an adequate number of very long-term survivors are still needed to realize the complete risks and impact of late mortality following autologous HCT for AML.
Our study has the limitations of a retrospective cohort design. Our results are also not generalizable to all patients who receive an autologous HCT for AML since our study was restricted to patients who received their transplant in CR1 and CR2. Also, only 4% of patients had poor-risk cytogenetics. Cytogenetic risk information from diagnosis was missing for 22% of patients; this was comprised primarily of patients from the earliest time period when cytogenetics were not routinely assessed in AML. In addition, the choice of autologous HCT as consolidation therapy over chemotherapy only or allogeneic HCT was determined by physicians at transplant centers. Factors that may have determined choice of therapy were not available to us for analysis.

Our study was not designed to determine the general outcomes of autologous HCT for AML since our cohort was restricted to AML patients in CR1 and CR2 who survived in remission for 2-years or more after autologous HCT. A large number of patients who receive an autologous HCT for AML relapse within the first 2-years post-transplant; in fact, among the 958 patients who received an autologous HCT for AML in CR1 or CR2 and were reported to the CIBMTR during the study period, 56% had treatment failure (relapse or death) within the first two years. Our specific objective was to determine long-term outcomes in patients who had survived 2-years or more and had presumably overcome the risks of initial relapse.

In conclusion, our study highlights the very favorable long-term survival among AML patients who receive an autologous HCT in CR1 or CR2 and survive in continuous complete remission for at least 2 years. Their mortality rates are similar to that of the general population.

ACKNOWLEDGEMENTS

The CIBMTR is supported by Public Health Service Grant/Cooperative Agreement U24-CA76518 from the National Cancer Institute (NCI), the National Heart, Lung and Blood Institute (NHLBI) and the National Institute of Allergy and Infectious Diseases (NIAID); a Grant/Cooperative Agreement 5U01HL069294 from NHLBI and NCI; a contract HHSH234200637015C with Health Resources and Services Administration (HRSA/DHHS); two Grants N00014-06-1-0704 and N00014-08-1-0058 from the Office of Naval Research; and grants from AABB; Aetna; American Society for Blood and Marrow Transplantation; Amgen, Inc.; Anonymous donation to the Medical College of Wisconsin; Astellas Pharma US, Inc.; Baxter International, Inc.; Bayer HealthCare Pharmaceuticals; Be the Match Foundation; Biogen IDEC; BioMarin Pharmaceutical, Inc.; Biovitrum AB; BloodCenter of Wisconsin; Blue Cross and Blue Shield Association; Bone Marrow Foundation; Canadian Blood and Marrow Transplant Group; CaridianBCT; Celgene Corporation; CellGenix, GmbH; Centers for Disease Control and Prevention; Children’s Leukemia Research Association; CInnImmuine Labs; CTI Clinical Trial and Consulting Services; Cubist Pharmaceuticals; Cylex Inc.; CytoTherm; DOR BioPharma, Inc.; Dynal Biotech, Inc.; Enix Company; Eisai, Inc.; Enzon Pharmaceuticals, Inc.; European Group for Blood and Marrow Transplantation; Gamida Cell, Ltd.; GE Healthcare; Genentech, Inc.; Genzyme Corporation; Histogenetics, Inc.; HKS Medical Information Systems; Hospira, Inc.; Infectious Diseases Society of America; Kiadis Pharma; Kirin Brewery Co., Ltd.; The Leukemia & Lymphoma Society; Merck & Company; The Medical College of Wisconsin; MGI Pharma, Inc.; Michigan Community Blood Centers; Millennium Pharmaceuticals, Inc.; Miller Pharmacal Group; Milliman USA, Inc.; Millenyi Biotec, Inc.; National Marrow Donor Program; Nature Publishing Group; New York Blood Center; Novartis Oncology; Oncology Nursing Society; Osiris Therapeutics, Inc.; Otsuka America Pharmaceutical, Inc.; Pall Life Sciences; Pfizer Inc.; Saladax Biomedical, Inc.; Schering Corporation; Society for Healthcare Epidemiology of America; StemCyte, Inc.; StemSoft Software, Inc.; Sysmex America, Inc.; Teva Pharmaceutical Industries; THERAKOS, Inc.; Thermogenesis Corporation; Vidacare Corporation; Vion Pharmaceuticals, Inc.; ViraCor Laboratories; ViroPharma, Inc.; and Wellpoint, Inc. The views expressed in this article do not reflect the official policy or position of the National Institute of Health, the Department of the Navy, the Department of Defense, or any other agency of the U.S. Government.
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Figure 1.
Overall survival of patients surviving in remission for at least 2-years after autologous hematopoietic-cell transplant for acute myeloid leukemia (by disease status at transplant)
Figure 2.
Non-relapse mortality among patients surviving in remission for at least 2-years after autologous hematopoietic-cell transplant for acute myeloid leukemia (by disease status at transplant)
Figure 3.
Relative excess mortality (solid line) compared to age-, gender- and race- matched general population for patients surviving in remission for at least 2-years after autologous hematopoietic-cell transplant for acute myeloid leukemia. A relative risk of 1 indicates that the mortality rate of the population of interest is similar to that of the general population. Dashed lines represent 95% pointwise confidence intervals. The population mortality rate is the same as that in our study cohort whenever the upper and lower 95% confidence bands include 1 in between them. From 4 years after transplantation, there was no difference in mortality rates between our study cohort and the matched general population. The confidence bands widen over time as fewer patients are at risk.
Table 1

Patient, disease and transplant characteristics of patients surviving in remission for at least 2 years after autologous hematopoietic-cell transplant for acute myeloid leukemia in first or second complete remission

| Characteristic                              | N (%)       |
|---------------------------------------------|-------------|
| Number of patients                          | 315         |
| Number of centers                           | 63          |
| Median age at transplant (range), years     | 34 (1-71)   |
| Age at transplant, years                    |             |
| <10                                         | 50 (16)     |
| 10-19                                       | 33 (10)     |
| 20-29                                       | 42 (13)     |
| 30-39                                       | 75 (24)     |
| 40-49                                       | 60 (19)     |
| 50-59                                       | 41 (13)     |
| ≥60                                         | 14 (4)      |
| Male gender                                 | 157 (50)    |
| Race                                        |             |
| White                                       | 271 (86)    |
| Black                                       | 19 (6)      |
| Other                                       | 25 (8)      |
| Country                                     |             |
| USA                                         | 262 (83)    |
| Canada                                      | 53 (17)     |
| Karnofsky score prior transplant            |             |
| ≥90                                         | 238 (76)    |
| < 90                                        | 61 (19)     |
| Missing                                     | 10 (2)      |
| Disease status at transplant                |             |
| CR1                                         | 246 (78)    |
| CR2                                         | 69 (22)     |
| Median WBC count at diagnosis (range), × 10^9/L | 11 (<1-400) |
| WBC count at diagnosis                      |             |
| <100,000                                    | 230 (73)    |
| ≥100,000                                    | 33 (10)     |
| Missing                                     | 52 (17)     |
| Cytogenetic risk at diagnosis               |             |
| Good prognosis                              | 62 (20)     |
| Intermediate prognosis                      | 169 (54)    |
| Poor prognosis                              | 14 (4)      |
| Unknown                                     | 70 (22)     |
| Number of chemotherapy regimens to achieve CR1 |         |
| 1                                           | 198 (63)    |

*Bone Marrow Transplant. Author manuscript; available in PMC 2011 September 01.*
| Characteristic                                                                 | N (%)  |
|-------------------------------------------------------------------------------|--------|
| **2**                                                                         | 71 (23) |
| ≥3                                                                            | 24 (8)  |
| Missing                                                                       | 22 (7)  |
| **Number of cycles of consolidation chemotherapy pre-transplant**             |        |
| No consolidation                                                             | 53 (17) |
| 1                                                                             | 101 (32) |
| ≥2                                                                            | 115 (37) |
| Missing                                                                       | 46 (15) |
| **Use of cytarabine in consolidation chemotherapy**                           |        |
| No consolidation                                                             | 53 (17) |
| Cytarabine                                                                   | 99 (31) |
| Other                                                                         | 156 (50) |
| Missing                                                                       | 7 (2)   |
| **Central nervous system involvement**                                       |        |
| Yes                                                                           | 30 (10) |
| No                                                                            | 270 (86) |
| Missing                                                                       | 15 (5)  |
| **Median time from diagnosis to transplant (range), months**                  | 6 (2-61) |
| **Time from diagnosis to transplant, months,**                                |        |
| < 6                                                                           | 149 (47) |
| ≥6                                                                            | 166 (53) |
| **Use of total body irradiation in conditioning**                             |        |
| Yes                                                                           | 77 (24) |
| No                                                                            | 235 (75) |
| Missing                                                                       | 3 (1)   |
| **Purging of graft**                                                          |        |
| Yes                                                                           | 140 (44) |
| No                                                                            | 173 (55) |
| Missing                                                                       | 2 (1)   |
| **Type of graft**                                                             |        |
| Bone marrow                                                                   | 226 (72) |
| Peripheral blood                                                              | 63 (20)  |
| Peripheral blood + bone marrow                                                | 26 (8)   |
| **Year of transplant**                                                       |        |
| 1990-1992                                                                     | 123 (39) |
| 1993-1995                                                                     | 125 (40) |
| 1996-1998                                                                     | 67 (21)  |
| **Hematopoietic growth factors to promote engraftment post-transplant**      |        |
| Yes                                                                           | 104 (33) |
| No                                                                            | 196 (62) |
| Missing                                                                       | 15 (5)   |
| **Median follow-up of survivors (range), months**                             | 106 (24-192) |
Abbreviations: CR – complete remission, WBC – white blood cell, GM-CSF – granulocyte-macrophage colony stimulating factor, G-CSF – granulocyte colony stimulating factor
Table 2

Variables tested in Cox-proportional hazards regression models

| Variable                                                                 | Reference Group   | Comparison 1               | Comparison 2               | Comparison 3               |
|-------------------------------------------------------------------------|-------------------|---------------------------|---------------------------|---------------------------|
| Age: <20 years vs. 20-49 years vs. ≥50 years                            |                   |                            |                            |                            |
| Gender: female vs. male                                                  |                   |                            |                            |                            |
| Race: White vs. Black vs. other                                          |                   |                            |                            |                            |
| Karnofsky performance score at transplant: ≥90 vs. <90                  |                   |                            |                            |                            |
| Year of transplant: 1990-92 vs. 1993-95 vs. 1996-98                      |                   |                            |                            |                            |
| Pre-transplant disease status: CR1 vs. CR2                              |                   |                            |                            |                            |
| Cytogenetic risk group at diagnosis: good vs. intermediate vs. poor     |                   |                            |                            |                            |
| WBC count at diagnosis: < 100,000 × 10^9/L vs. ≥100,000 × 10^9/L        |                   |                            |                            |                            |
| History of central nervous system involvement: no vs. yes               |                   |                            |                            |                            |
| Number of regimens to achieve CR1: 1 vs. 2 vs. ≥3                       |                   |                            |                            |                            |
| Number of cycles of consolidation therapy after CR: 0 vs. 1 vs. ≥2      |                   |                            |                            |                            |
| Use of high-dose cytarabine for induction or consolidation: no vs. yes  |                   |                            |                            |                            |
| Use of total body irradiation in conditioning regimen: no vs. yes       |                   |                            |                            |                            |
| Graft purging: no vs. yes                                               |                   |                            |                            |                            |
| Graft source: bone marrow vs. peripheral blood                          |                   |                            |                            |                            |
| Use of hematopoietic growth factors to promote engraftment post-transplant: no vs. yes |                   |                            |                            |                            |

Abbreviations: CR – complete remission, WBC – white blood cell, GM-CSF – granulocyte-macrophage colony stimulating factor, G-CSF – granulocyte colony stimulating factor.

*Reference group
Table 3

Univariate probabilities for transplant outcomes of patients surviving in remission for at least 2 years after autologous transplant for acute myeloid leukemia

| Outcome                        | CR1               |         | CR2               |         |
|--------------------------------|-------------------|---------|-------------------|---------|
|                                | N     | % (95% CI) | N     | % (95% CI)       |
|--------------------------------|------|------------|------|-----------------|
| Overall survival               | 246  | 69         | 98   | 96-100          |
|                                |      |            |      | 91 (82-97)      |
| 5 years                        |      |            |      |                 |
| 10 years                       |      |            |      |                 |
| Disease-free survival          | 246  | 67         | 94   | 91-97           |
|                                |      |            |      | 88 (78-94)      |
| 5 years                        |      |            |      |                 |
| 10 years                       |      |            |      |                 |
| Relapse                        | 246  | 67         | 4    | 2-7             |
|                                |      |            |      | 6 (2-13)        |
| 5 years                        |      |            |      |                 |
| 10 years                       |      |            |      |                 |
| Non-relapse mortality          | 246  | 67         | 1    | 0-3             |
|                                |      |            |      | 6 (2-13)        |
| 5 years                        |      |            |      |                 |
| 10 years                       |      |            |      |                 |

Abbreviations: CR – complete remission

aFrom the date of transplant
Table 4
Multivariate outcomes of patients surviving in remission for at least 2 years after autologous hematopoietic-cell transplant for lymphoma

| Outcomes and variables          | N   | Relative risk (95% CI) | P-value |
|--------------------------------|-----|------------------------|---------|
| Overall survival               |     |                        |         |
| Age at transplant              |     |                        |         |
| <20 years                      | 83  | 1.00                   | 0.002 a |
| 20-49 years                    | 177 | 11.43 (1.37-95.61)     | 0.025   |
| ≥50 years                      | 53  | 32.44 (3.78-278.4)     | 0.002   |
| Cytogenetic risk               |     |                        |         |
| Good prognosis                 | 62  | 1.00                   |         |
| Intermediate prognosis         | 168 | 2.34 (0.66-8.31)       | 0.188   |
| Poor prognosis                 | 14  | 12.43 (1.91-81.00)     | 0.008   |
| Disease status at transplant   |     |                        |         |
| CR1                            | 246 | 1.00                   |         |
| CR2                            | 67  | 3.81 (1.59-9.12)       | 0.003   |
| Disease free survival          |     |                        |         |
| Age at transplant              |     |                        |         |
| <20 years                      | 83  | 1.00                   | 0.006 a |
| 20-49 years                    | 177 | 7.95 (1.79-35.29)      | 0.006   |
| ≥50 years                      | 53  | 12.52 (2.64-59.47)     | 0.002   |
| Cytogenetic risk               |     |                        |         |
| Good prognosis                 | 62  | 1.00                   |         |
| Intermediate prognosis         | 168 | 3.34 (0.99-11.35)      | 0.053   |
| Poor prognosis                 | 14  | 11.69 (2.27-60.21)     | 0.003   |
| Disease status                 |     |                        |         |
| CR1                            | 246 | 1.00                   |         |
| CR2                            | 67  | 2.10 (1.01-4.39)       | 0.010   |
| Relapse                        |     |                        |         |
| Hematopoietic growth factors to promote engraftment post-transplant | | | |
| No                             | 196 | 1.00                   |         |
| Yes                            | 102 | 3.64 (1.32-10.05)      | 0.013   |
| Non-relapse mortality          |     |                        |         |
| Karnofsky score prior to transplant | | | |
| ≥90                            | 236 | 1.00                   |         |
| <90                            | 61  | 4.02 (1.51-10.73)      | 0.005   |

Abbreviations: CR – complete remission, GM-CSF – granulocyte-macrophage colony stimulating factor, G-CSF – granulocyte colony stimulating factor

a Multiple degree of freedom test for equality over categories