

TRANSPLANTATION OF BONE MARROW AS COMPARED WITH PERIPHERAL-BLOOD CELLS FROM HLA-IDENTICAL RELATIVES IN PATIENTS WITH HEMATOLOGIC CANCERS

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ABSTRACT

Background In recipients of allogeneic hematopoietic-cell transplants, peripheral-blood cells mobilized with the use of filgrastim (recombinant granulocyte colony-stimulating factor) engraft more rapidly than bone marrow. However, the relative effects of these techniques on the rates of acute and chronic graft-versus-host disease, overall survival, and disease-free survival have not been determined in randomized studies.

Methods Between March 1996 and July 1999, 172 patients (12 to 55 years of age) with hematologic cancer were randomly assigned to receive either bone marrow or filgrastim-mobilized peripheral-blood cells from HLA-identical relatives for hematopoietic rescue after the treatment of hematologic cancer with high doses of chemotherapy, with or without radiation.

Results The recovery of both neutrophils and platelets was faster with peripheral-blood cells than with marrow ($P < 0.001$ for both comparisons). The cumulative incidence of grade II, III, or IV acute graft-versus-host disease at 100 days was 64 percent with peripheral-blood cells and 57 percent with marrow (hazard ratio, 1.21; 95 percent confidence interval, 0.81 to 1.81; $P = 0.35$). The cumulative incidence of chronic graft-versus-host disease was 46 percent with peripheral-blood cells and 35 percent with marrow (hazard ratio, 1.16; 95 percent confidence interval, 0.71 to 1.90; $P = 0.54$). The estimated overall probability of survival at two years was 66 percent with peripheral-blood cells and 54 percent with marrow (hazard ratio for death, 0.62; 95 percent confidence interval, 0.38 to 1.02; $P = 0.06$). The rate of disease-free survival at two years was 65 percent with peripheral-blood cells and 45 percent with marrow (hazard ratio for relapse or death, 0.60; 95 percent confidence interval, 0.38 to 0.95; $P = 0.03$).

Conclusions In patients given high-dose chemotherapy, with or without radiation, for the treatment of hematologic cancer, allogeneic peripheral-blood cells used for hematopoietic rescue restore blood counts faster than allogeneic bone marrow, without increasing the risk of graft-versus-host disease. (N Engl J Med 2001;344:175-81.)

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HEMATOPOIETIC cells reside predominantly in the bone marrow but can be mobilized in large numbers in the blood by the administration of filgrastim (recombinant granulocyte colony-stimulating factor [G-CSF]). Apheresis products containing G-CSF-mobilized peripheral-blood cells are now widely used instead of bone marrow for autologous transplantation.¹ Peripheral-blood cells engender hematopoietic recovery after transplantation more rapidly than does marrow. These favorable results with autologous cells prompted phase 1 and 2 evaluations of the use of allogeneic peripheral-blood cells for hematopoietic rescue.²⁻⁴ The results of these studies, which used historical controls, suggested that the recovery of neutrophils, red cells, and platelets was faster with the use of peripheral-blood cells than with the use of marrow, with no apparent increase in the incidence of acute graft-versus-host disease (GVHD).⁵⁻⁷ In these retrospective analyses, however, the outcomes with respect to chronic GVHD, relapse, and survival were conflicting.⁸⁻¹⁴

In 1995, we initiated a multicenter, randomized trial to compare the use of allogeneic marrow with the use of peripheral-blood cells from HLA-identical related donors with respect to the incidence of acute and chronic GVHD and to confirm that engraftment occurs more rapidly with peripheral-blood cells than with bone marrow. Since the initiation of this trial, the results of four randomized studies, each involving 37 to 100 patients, have been reported.¹⁵⁻¹⁸ These trials found that engraftment with peripheral-blood cells was more rapid, but because of the size and design of the studies, questions remained about the relative effects of peripheral-blood cells and marrow on the incidence of chronic GVHD and on rates of relapse and survival.

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METHODS

Study Design

This trial was conducted at the Fred Hutchinson Cancer Research Center (Seattle), Stanford University Medical Center (Stanford, Calif.), and City of Hope Medical Center (Duarte, Calif.). A single study protocol was reviewed and approved by the institutional review boards of the participating centers. Eligible patients (or their parents or guardians) and their donors gave written informed consent before randomization.

Patients between the ages of 12 and 55 years were eligible for the study if they had a hematologic cancer for which allogeneic transplantation of marrow or peripheral-blood cells from an HLA-identical, related donor who was at least 12 years old was indicated. Enrollment criteria included a serum creatinine concentration of less than 1.5 mg per deciliter (133 μ mol per liter), a cardiac ejection fraction of more than 45 percent, a corrected pulmonary carbon monoxide diffusing capacity that was more than 50 percent of the predicted value, and results on liver-function tests that were less than twice the upper limit of normal. Donors were required to have normal results on physical examination, normal serum chemical values, normal blood counts, and negative results on serologic testing for the human immunodeficiency virus and hepatitis B; premenopausal female donors were also required to have a negative result on a pregnancy test.

After random assignment to transplantation with peripheral-blood cells or bone marrow, the patients were stratified according to treatment center, age (≤ 30 or > 30 years), and stage of cancer (less advanced or more advanced). Within these strata, assignments were balanced in blocks of random size. Less advanced cancers were defined as acute myeloid leukemia or acute lymphoblastic leukemia in first remission; chronic myeloid leukemia in a chronic phase; lymphoma in first remission, untreated first relapse, or second remission; and refractory anemia without excess blasts. All other stages of these cancers and all other types of hematologic cancers were considered more advanced disease.

Disease-specific conditioning regimens were administered before transplantation, according to the usual protocols at each institution, and included high-dose chemotherapy with or without total-body irradiation (total dose, 12 to 13.5 Gy). Marrow was collected from the donor by standard techniques on the day of infusion. After treatment of the donor with subcutaneous G-CSF at a dose of 16 μ g per kilogram of body weight, given once daily for five days, peripheral-blood cells were collected by apheresis beginning one day before the infusion of cells into the recipient. This dose has been reported to provide satisfactory mobilization of cells and to be tolerated well.¹⁹ The cells were stored overnight at 4°C. If the first apheresis procedure resulted in the collection of at least 5.0×10^6 CD34+ cells per kilogram of the recipient's body weight, the cells were infused the next day, with no further apheresis of cells from the donor. If the first procedure resulted in the collection of fewer than 5.0×10^6 CD34+ cells per kilogram of the recipient's body weight, a second procedure was performed the next day, and cells from both collections were infused on that day.

Methotrexate and cyclosporine were given for the prevention of GVHD.²⁰ Cases of acute or chronic GVHD were diagnosed and managed according to methods described previously.^{21,22} Antibiotics were administered according to the usual policies at each center to prevent bacterial, fungal, and viral infections. Patients were treated with G-CSF only when myeloid engraftment was delayed or impaired.

The day of neutrophil engraftment was defined as the first of three consecutive days on which the patient's absolute neutrophil count was above 500 per cubic millimeter. The day of platelet engraftment was defined as the first of seven consecutive days on which the platelet count was above 20,000 per cubic millimeter without platelet transfusion.

The primary end point of the study was grade II, III, or IV acute GVHD within the first 100 days after transplantation. Acute GVHD was graded according to standard criteria.²¹ Our null hy-

pothesis was that the incidence of acute GVHD in patients who received peripheral-blood cells would be at least 10 percent greater than the incidence in those who received bone marrow, and we sought to reject that hypothesis. An analysis of historical data suggested that the incidence of acute GVHD might be as much as 20 percent lower with peripheral-blood cells than with marrow. A total of 200 patients, with random assignment of 100 to each group, would be required to provide the study with 89 percent power to reject the null hypothesis at the one-sided 0.05 level of significance if the incidence of acute GVHD with peripheral-blood cells was in fact 10 percent lower than the incidence with marrow. Similarly, if we used a standard null hypothesis of equal incidence in the two groups and a two-sided 0.05 level of significance, the power of the study would be 81 percent to detect a true difference of 20 percent between the rates in the two groups. We planned to undertake an interim analysis after 100 patients had been evaluated for the grade of acute GVHD, with a provision to stop the study early if the null hypothesis could be rejected at the 0.01 level of significance. There was also a provision to stop the study early if the rate of chronic GVHD in the group given peripheral-blood cells was more than 10 percent higher than that in the group given bone marrow at the one-sided 0.05 level of significance.

After 100 patients had been enrolled in the study, a data and safety monitoring committee undertook an interim analysis. This analysis, completed in June 1999, included data on acute GVHD in these initial 100 patients and data on survival in the 138 patients who underwent transplantation through February 1999. Neither of the predefined criteria for stopping the study was met; however, a review of available mortality data indicated a highly significant difference in survival that favored the group given peripheral-blood cells ($P=0.002$, by the likelihood-ratio test for a proportional-hazards model). According to the recommendation of the committee, the study was closed to new patients early, in July 1999, at which time 175 patients had been enrolled. This report includes data on these 175 patients, with all available follow-up data through June 2000.

Statistical Analysis

Estimates of overall survival and disease-free survival were calculated with use of the Kaplan–Meier method.²³ The cumulative rates of acute and chronic GVHD, relapse, and transplantation-related death were computed according to the method described by Kalbfleisch and Prentice.²⁴ The statistical significance of differences in these end points between the two groups was calculated with use of the likelihood-ratio statistic for proportional-hazards regression models, with adjustment for risk factors where appropriate. Hazard ratios were estimated from these models, in which patients were stratified according to center, risk (more or less advanced disease), and age (≤ 30 or > 30 years). The significance of differences between the two groups in the numbers of cells administered, the time to engraftment, and the number of transfusions required was evaluated with the use of two-sample *t*-tests; the specific methods of evaluation were not prespecified and followed usual statistical practice. All comparisons were performed according to the intention-to-treat principle and tested a null hypothesis of equivalence between the two groups. All *P* values are two-sided. The *P* values and confidence intervals reported do not reflect any effects of the interim analysis or early closure of the study.

RESULTS

Characteristics of the Patients

A total of 175 patients consented to participate and were randomly assigned to one of the two study groups. Shortly after randomization but before the beginning of treatment, three patients were found to be ineligible (one assigned to receive marrow and two assigned to receive peripheral-blood cells) and were given alternative therapy; the results for these three

patients were excluded from further analysis. Five other patients withdrew after randomization: two because of their physicians' preference, two because of their own preference, and one because the donor withdrew consent. Three of these five patients had been assigned to receive marrow but received peripheral-blood cells instead, and two of them had been assigned to receive peripheral-blood cells but received marrow instead. The results for these five patients were included in the intention-to-treat analysis according to their randomly assigned treatment. There were no significant differences between the two groups of patients with respect to their base-line characteristics (Table 1) or the conditioning regimens they received before transplantation (Table 2).

Blood-Cell Harvest

Bone marrow was collected from 90 donors without incident. Peripheral-blood cells were collected from 82 donors, 55 with a single apheresis proce-

TABLE 1. CHARACTERISTICS OF THE PATIENTS, ACCORDING TO TREATMENT ASSIGNMENT.*

CHARACTERISTIC	PERIPHERAL-BLOOD CELLS (N=81)	BONE MARROW (N=91)
Diagnosis — no. (%)		
Acute myeloid leukemia	15 (19)	22 (24)
Acute lymphoblastic leukemia	12 (15)	10 (11)
Non-Hodgkin's lymphoma	13 (16)	10 (11)
Hodgkin's lymphoma	0	1 (1)
Chronic myeloid leukemia	22 (27)	35 (38)
Multiple myeloma	5 (6)	1 (1)
Myelodysplasia	13 (16)	10 (11)
Chronic lymphocytic leukemia	0	1 (1)
Waldenström's disease	0	1 (1)
Mycosis fungoides	1 (1)	0
Disease status — no. (%)		
Less advanced	41 (51)	51 (56)
More advanced	40 (49)	40 (44)
Sex — no. (%)		
Male, with male donor	28 (35)	40 (44)
Male, with female donor	28 (35)	22 (24)
Female, with female donor	13 (16)	19 (21)
Female, with male donor	12 (15)	10 (11)
Cytomegalovirus status — no. (%)		
Seropositive, with seropositive donor	30 (37)	35 (38)
Seropositive, with seronegative donor	16 (20)	15 (16)
Seronegative, with seronegative donor	20 (25)	27 (30)
Seronegative, with seropositive donor	15 (19)	14 (15)
Age — yr		
Recipient		
Median	42	42
Range	15–55	12–55
Donor		
Median	40	40
Range	12–62	15–63

*Because of rounding, not all percentages total 100.

TABLE 2. CONDITIONING REGIMENS USED BEFORE TRANSPLANTATION, ACCORDING TO TREATMENT ASSIGNMENT.*

REGIMEN	PERIPHERAL-BLOOD CELLS (N=81)	BONE MARROW (N=91)
	no. (%)	
Total-body irradiation and chemotherapy		
Busulfan	12 (15)	13 (14)
Cyclophosphamide	24 (30)	30 (33)
Etoposide	13 (16)	7 (8)
Busulfan and cyclophosphamide	3 (4)	0
Chemotherapy alone		
Busulfan and cyclophosphamide	29 (36)	40 (44)
Busulfan and thiopeta	0	1 (1)

*Because of rounding, not all percentages total 100. There were no significant differences between the two groups in any of the variables.

dure, 25 with two apheresis procedures, 1 with three procedures, and 1 with four procedures. The collections that required three or four apheresis procedures were considered protocol violations. After two collections, the apheresis products from six donors contained fewer than 5.0×10^6 CD34+ cells per kilogram of the patient's body weight. Of these six products, five contained more than 4.0×10^6 CD34+ cells per kilogram, and one contained only 1.0×10^6 CD34+ cells per kilogram; in the latter case, marrow was then collected from the donor and infused with the peripheral-blood cells. Histologic evaluation of marrow from this donor revealed myelodysplasia.²⁵ Data from the two patients who received peripheral-blood cells from more than two collections and from the single patient who received both peripheral-blood cells and marrow were included with those of the peripheral-blood cell group, according to these patients' original random assignment. The blood-cell grafts contained approximately 5, 3, and 12 times the numbers of nucleated cells, CD34+ cells, and CD3+ T cells, respectively, that were present in the marrow grafts (Table 3).

Time to Engraftment and Transfusion Requirements

Absolute neutrophil counts exceeded 500 per cubic millimeter five days earlier in the patients assigned to receive peripheral-blood cells than in the patients assigned to receive bone marrow ($P < 0.001$) (Table 4). Similarly, platelet counts exceeded 20,000 per cubic millimeter, without the need for transfusions, six days earlier in the peripheral-blood-cell group than in the bone marrow group ($P < 0.001$). Fewer units of platelets were transfused in the peripheral-blood-cell group than in the bone marrow group ($P = 0.003$), but the two groups received a similar number of units of red cells.

TABLE 3. CHARACTERISTICS OF THE TRANSPLANTED CELLS, ACCORDING TO PATIENTS' TREATMENT ASSIGNMENT.*

CHARACTERISTIC	PERIPHERAL-BLOOD CELLS (N=81)	BONE MARROW (N=91)†
	per kilogram	
Total nucleated cells ($\times 10^{-8}$)		
Median	11.6	2.3
Range	1.5–24.6	0.02–14.6
CD34+ cells ($\times 10^{-6}$)		
Median	7.3	2.4
Range	1.0–29.8	0.8–10.4
CD3+ cells ($\times 10^{-6}$)		
Median	279	23.8
Range	143–788	5.4–347
Volume (ml)		
Median	4.0	12.2
Range	1.5–11.3	1.2–30.5

*All values are expressed per kilogram of the recipient's body weight. CD34 is a marker of hematopoietic stem cells, and CD3 is a marker present on all T cells. $P < 0.001$ for all four comparisons.

†Values for CD34+ cells and CD3+ cells were not available for eight of the patients assigned to receive marrow.

TABLE 4. TIME TO ENGRAFTMENT AND TRANSFUSION REQUIREMENTS, ACCORDING TO TREATMENT ASSIGNMENT.

VARIABLE	PERIPHERAL-BLOOD CELLS (N=81)	BONE MARROW (N=91)	P VALUE
Time to engraftment (days)			
Neutrophils $> 500/\text{mm}^3$			< 0.001
Median	16	21	
Range	11–29	13–36	
Platelets $> 20,000/\text{mm}^3$			< 0.001
Median	13	19	
Range	5–41	7–74	
Transfusion (no. of units)			
Red cells			0.32
Median	6	6	
Range	0–64	0–158	
Platelets			0.003
Median	30	46	
Range	3–168	10–396	

Acute and Chronic GVHD

The incidence of grade II, III, or IV acute GVHD was similar in the two study groups (hazard ratio for the peripheral-blood–cell group vs. the bone marrow group, 1.21; 95 percent confidence interval, 0.81 to 1.81; $P = 0.35$). The cumulative incidence of grade II, III, or IV acute GVHD at 100 days was 64 percent in the peripheral-blood–cell group and 57 percent

in the bone marrow group. The two groups were also similar in terms of the rates of grade III or IV acute GVHD (hazard ratio for the peripheral-blood–cell group vs. the bone marrow group, 1.27; 95 percent confidence interval, 0.55 to 2.89; $P = 0.57$). The cumulative incidence of grade III or IV acute GVHD at 100 days was 15 percent in the peripheral-blood–cell group and 12 percent in the bone marrow group.

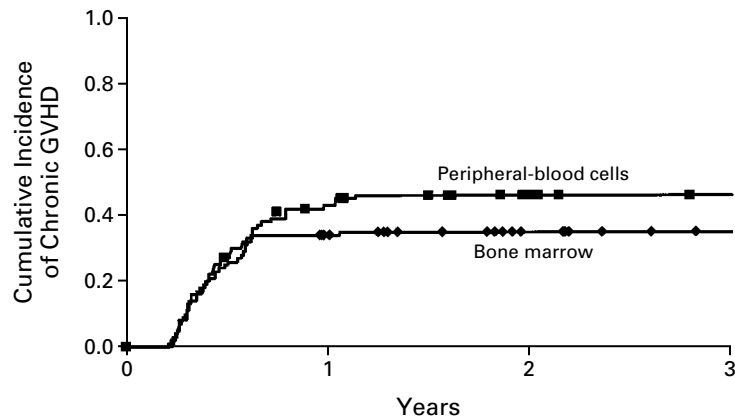
Extensive, chronic GVHD occurred in 37 of the patients assigned to receive peripheral-blood cells as compared with 32 of those assigned to receive bone marrow. The cumulative incidence of extensive, chronic GVHD at two years was 46 percent in the peripheral-blood–cell group and 35 percent in the bone marrow group (hazard ratio, 1.16; 95 percent confidence interval, 0.71 to 1.90; $P = 0.54$) (Fig. 1).

Rates of Death, Relapse, and Survival

Of the 81 patients assigned to receive peripheral-blood cells, 29 died during the follow-up period, as compared with 42 of the 91 patients in the bone marrow group. The predominant causes of death in the bone marrow group were noninfectious pneumonia and recurrent disease (Table 5). There was no difference between the two groups in the number of nonfatal infections. The cumulative incidence of transplantation-related death at two years was 21 percent in the peripheral-blood–cell group and 30 percent in the bone marrow group (hazard ratio, 0.70; 95 percent confidence interval, 0.38 to 1.28; $P = 0.24$). The cumulative incidence of relapse at two years was 14 percent in the peripheral-blood–cell group and 25 percent in the bone marrow group (hazard ratio, 0.49; 95 percent confidence interval, 0.24 to 1.00; $P = 0.04$).

The median follow-up time for all the surviving patients was 26 months (range, 9 to 47). The estimated probability of survival at two years was 66 percent in the peripheral-blood–cell group, as compared with 54 percent in the bone marrow group (hazard ratio for death, 0.62; 95 percent confidence interval, 0.38 to 1.02; $P = 0.06$) (Fig. 2). The rate of disease-free survival for all the patients at two years was 65 percent in the peripheral-blood–cell group, as compared with 45 percent in the bone marrow group (hazard ratio for relapse or death, 0.60; 95 percent confidence interval, 0.38 to 0.95; $P = 0.03$).

In the subgroup of patients with less advanced cancer, the estimated probability of survival at two years was 75 percent among those assigned to receive peripheral-blood cells and 72 percent among those assigned to receive bone marrow (hazard ratio for death, 0.82; 95 percent confidence interval, 0.36 to 1.85; $P = 0.63$). In the subgroup of patients with more advanced cancer, the estimated probability of survival at two years was 57 percent among those assigned to receive peripheral-blood cells and 33 percent among those assigned to receive marrow (hazard ratio for death, 0.54; 95 percent confidence interval, 0.29 to



No. AT RISK		0	1	2	3
Peripheral-blood cells	81		24	12	8
Bone marrow	91		27	13	5

Figure 1. Cumulative Incidence of Chronic Graft-versus-Host Disease (GVHD) in the Two Study Groups. Among the patients randomly assigned to receive peripheral-blood cells, the cumulative incidence of chronic GVHD at two years was 46 percent, as compared with 35 percent among those assigned to receive bone marrow.

TABLE 5. CAUSES OF DEATH DURING FOLLOW-UP, ACCORDING TO TREATMENT ASSIGNMENT.

CAUSE	PERIPHERAL-BLOOD CELLS (N=81)	BONE MARROW (N=91)
	no. of patients	
Noninfectious pneumonia	7	13
Veno-occlusive disease of the liver	1	1
Multiorgan failure	2	2
Hemorrhage	1	1
Cardiac failure	1	1
Graft-versus-host disease	3	3
Infection	4	6
Sepsis	2	2
Fungal	0	2
Viral	2	2
Recurrent disease	10	15
Total	29	42

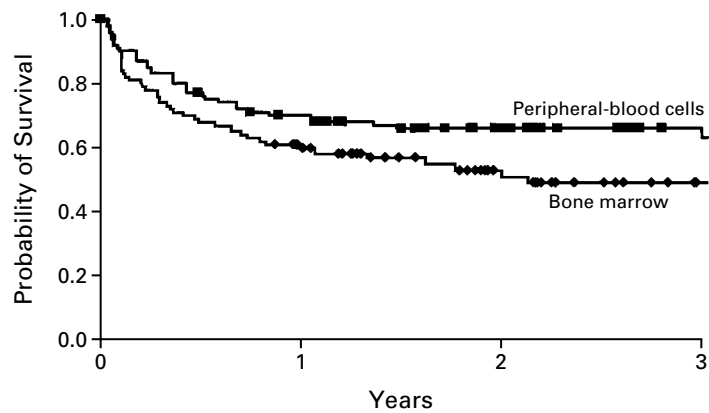
0.99; $P=0.04$). The interaction between the stage of disease and the type of graft was not statistically significant ($P=0.42$).

DISCUSSION

In this randomized trial, the transplantation of allogeneic peripheral-blood cells after high-dose chemotherapy for the treatment of hematologic cancer was associated with faster recovery of neutrophils and platelets and with the transfusion of fewer units of

platelets than was the transplantation of allogeneic bone marrow. These results are similar to those generally observed with autologous hematopoietic cells. Even though the number of CD3+ cells (i.e., T cells) in the peripheral-blood-cell transplants was 12 times that in the marrow transplants, the rates of acute and chronic GVHD were not significantly higher in the group that received peripheral-blood cells. Our results suggest that the transplantation of peripheral-blood cells may offer advantages over the transplantation of bone marrow in terms of overall survival and disease-free survival. These benefits were seen primarily among the patients with advanced hematologic cancer and may be related to the lower risks of interstitial pneumonia and recurrent disease with peripheral-blood-cell transplantation. This finding is in agreement with those of a retrospective registry analysis in which the rate of survival was higher among patients with advanced hematologic cancer who received peripheral-blood cells rather than marrow.¹⁴

Four randomized studies, the largest of which involved 100 patients, have compared peripheral-blood cells with bone marrow for hematopoietic rescue after high-dose chemotherapy.¹⁵⁻¹⁸ In all four studies, platelet recovery occurred earlier — and in three, neutrophil recovery also occurred earlier — in the patients who received peripheral-blood cells than in those who received marrow. In the fourth study, the time to neutrophil recovery was similar in the two groups. In all four studies, the risk of acute GVHD was similar in recipients of peripheral-blood cells and recipients of marrow. In two of the four studies, the risk of chronic



No. AT RISK	
Peripheral-blood cells	81 53 35 21
Bone marrow	91 48 23 7

Figure 2. Probability of Survival in the Two Study Groups.

Among the patients randomly assigned to receive peripheral-blood cells, the probability of survival at two years was 66 percent, as compared with 54 percent among those assigned to receive bone marrow.

GVHD was higher among those who received peripheral-blood cells. These disparities might have been due to a variety of factors, including the small numbers of patients in each study and differences among the studies in the length of follow-up, the type of prophylaxis against GVHD, or the regimen of G-CSF used for the mobilization of peripheral-blood cells.

In two of the studies that reported a higher incidence of chronic GVHD with peripheral-blood cells than with bone marrow, methotrexate was omitted on day 11 after stem-cell transplantation. In patients who receive an allogeneic marrow graft, omission of the dose of methotrexate on day 11 increases the risk of acute GVHD.²⁰ Although this observation does not directly explain the higher incidence of chronic GVHD in patients who receive peripheral-blood cells, acute GVHD predisposes patients to the development of chronic GVHD. Recently, a large registry analysis reported a higher incidence of chronic GVHD among recipients of peripheral-blood cells (65 percent, vs. 53 percent among bone marrow recipients; $P=0.02$)¹⁴; this difference is similar in magnitude to that in our study.

In all the reported randomized studies, the dose of G-CSF was 10 μg per kilogram per day, which was lower than the dose of 16 μg per kilogram per day used in our study. Our regimen of G-CSF was chosen on the basis of data indicating that the yield of CD34+ cells is better with the higher dose, both for autologous transplantation and for allogeneic transplanta-

tion. In animal models and in clinical studies, G-CSF induces T cells to produce interleukin-4 and interleukin-10, rather than interleukin-2 and interferon- γ . Interleukin-4 and interleukin-10 (the profile of type 2 helper T cells) have been shown to down-regulate inflammatory responses, including that involved in GVHD, whereas interleukin-2 and interferon tend to be proinflammatory.^{26,27} Other work has shown that use of G-CSF mobilizes greater numbers of CD14+ monocytes with suppressor-cell function²⁸ and greater numbers of dendritic cells that induce a type 2 helper T-cell response.²⁹ Thus, the dose of G-CSF may influence the risk of chronic GVHD by inducing qualitative or quantitative changes in the cytokines produced by T cells from the donor.

The results of one randomized study and one retrospective study suggested that the transplantation of peripheral-blood cells rather than bone marrow after high-dose chemotherapy for hematologic cancer may be associated with a lower risk of relapse.^{18,30} We found a similar trend, although in our study the subgroups of patients with specific cancers were too small for individual analysis. The graft-versus-leukemia effect of allogeneic T cells has been reported to be particularly strong in patients with chronic myeloid leukemia and less obvious in those with other types of leukemia. Further studies are needed to answer questions about the antileukemic potency of peripheral-blood cells as compared with that of bone marrow.

Our study indicates that for allogeneic hematopoietic-cell transplantation, the use of peripheral-blood

cells rather than bone marrow results in higher rates of overall and disease-free survival. Moreover, we found that the patients in whom the benefit of peripheral-blood cells was most apparent were those with advanced hematologic cancer. However, since survival was not a prespecified end point in the original design of the study, these results must be interpreted with caution. Other studies have also shown that the use of peripheral-blood cells is associated with fewer days of hospitalization and lower overall costs.

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