Allogeneic Bone Marrow Transplantation With a Fixed Low Number of T Cells in the Marrow Graft

By Leo F. Verdonck, Adriaan W. Dekker, Gijsbert C. de Gast, M. Loes van Kempen, Henk M. Lokhorst, and H. Karel Nieuwenhuis

Despite prophylaxis with immunosuppressive drugs, severe acute graft-versus-host disease (GVHD) remains a major cause of morbidity and mortality in patients transplanted with unmodified bone marrow (BM) grafts from HLA-identical siblings. Although T-cell depletion of the BM graft has evolved as the most effective method to prevent severe acute GVHD, this beneficial effect is counterbalanced by an increased rate of graft failure and relapse of the disease. To find an approach to T-cell depletion that may avoid these extreme risks, we gave BM recipients a fixed low number of 1 × 10^6 donor T cells per kilogram of recipient’s body weight in the graft. This corresponds with 99% T-cell depletion and is achieved by the addition of T cells to the graft that was previously depleted of T cells. A total of 70 patients with hematologic malignancies or aplastic anemia, including 40 patients with standard-risk leukemias, received BM grafts, depleted of T cells according to this approach, from HLA-identical siblings. The preparative regimen consisted of cyclophosphamide and total body irradiation. The patients also received a short course of cyclosporine posttransplant. Graft failure did not occur. Acute GVHD, only grade I or II, was seen in 70% of the patients and was limited to the skin in all patients. Chronic GVHD occurred in 31% of the patients and, with the exception of 1 patient, was limited to the skin as well. Relapse occurred in 3 of 40 (8%) patients with standard-risk leukemias, resulting in a projected survival at 5 years of 80%. Patients with standard-risk diseases had a procedure-related mortality of 11%. Quality of life, determined 1 year after BM transplant, was good in almost all patients with standard-risk diseases. Thus, this approach of T-cell depletion may be an approach that avoids the development of severe acute and chronic GVHD without damaging the function or antileukemic effect of the graft and that has a low transplant-related morbidity and mortality.

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Submitted July 29, 1993; accepted January 21, 1994.

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BMT recipients develop significant acute GVHD.10-12 Although T-cell depletion decreases acute GVHD incidence and severity, this beneficial effect is counterbalanced by an increased rate of graft failure and of leukemia relapse. Graft failure occurs in 15% of T-cell-depleted BM grafts from HLA-identical siblings versus 1% in those receiving non–T-cell-depleted grafts.13-16 Because acute and chronic GVHD are associated with an antileukemic effect,17-21 methods aimed to decrease GVHD can be associated with an increased relapse rate. A large international study has recently shown that T-cell depletion increases the relapse rate both in patients with acute leukemias in first remission and in patients with chronic myeloid leukemias in first chronic phase.22 However, as follow-up increases, patients who were transplanted with unmodified BM grafts become more intensive posttransplant treatment with combinations of methotrexate and cyclosporine also have more relapses than do patients who receive monotherapy.14,15,22 Thus, approaches intended to decrease acute GVHD and, consequently, reduce transplant-related mortality, while avoiding more relapses and graft failures, are highly desirable and necessary if further progress in BMT is to be made.

To try to accomplish these goals, we started an approach of partial T-cell depletion, administering BM recipients a fixed low number of 1 × 10^6 T cells per kilogram of body weight in the graft. This was performed by the addition of T cells that were present in unmodified BM, which was taken apart during BM processing, to the BM graft that underwent maximal T-cell depletion.23 The fixed low number of 1 × 10^6 T cells per kilogram was chosen because it corresponded with approximately 99% T-cell depletion, a T-cell depletion probably effective for abrogation of severe acute GVHD.23-26 We considered the addition of unmanipulated T cells important to avoid both graft failure and the high relapse rate, which are the major drawbacks of maximal T-cell depletion. Preliminary results of this approach were encouraging.23 Here we report the results of this approach in 70 patients, including 40 patients with standard-risk leukemias, who were given HLA-identical BM grafts from siblings.
T-CELL DEPLETION IN ALLOGENEIC BM
tancies or aplastic anemia who received BM grafts from genotypi-
cally HLA-identical donors and were treated with cyclophosphamide
divided for risk of relapse into (1) high-risk patients (n = 26); acute
leukemias in first or second relapse (n = 7); advanced myelodysplas-
ty syndromes (n = 2); refractory multmyeloma, stage III (n = 10); refractory non-Hodgkin’s lymphomas (n = 3); chronic myeloid
leukemia (CML) in second or third chronic phase (n = 4) or (2)
standard-risk patients (n = 44): acute myeloblastic leukemia (AML)
in first remission (n = 13); acute lymphoblastic leukemia (ALL) in first
remission (n = 16) or in second remission (n = 2); CML in first
chronic phase (n = 9); severe aplastic anemia (n = 4). Clinical
data of the standard-risk leukemias (n = 40) are given in Table 2.

The conditioning regimen consisted of cyclophosphamide 60 mg/
kg body weight, infused on each of 2 successive days and was
followed in 7 patients by a single dose of 800 cGy of TBI (lung
dose, 700 cGy) and in 63 patients by 500 cGy or 600 cGy of TBI
(lung dose, 800 or 850 cGy) on each of 2 successive days. The
irradiation was delivered by a 10-MV linear accelerator at a rate of
12 cGy per minute. BM infusion occurred the day after or on the
same day of TBI.

All patients were hospitalized in conventional single rooms with
reversed isolation; all received infection prophylaxis with oral ci-
proflaxacin and amphotericin B20 together with oral acyclovir and,
during the first 10 days after transplant, with intravenous cefalothin.
Furthermore, they were administered parenteral alimentation and
semitestile food until the granulocyte counts were above 500/μL on
2 successive days, after which ciprofloxacin, amphotericin, and the
reversed isolation were stopped, and prophylaxis with cotrimoxazole
was started and continued for 6 months (together with acyclovir
prophylaxis) after BMT. Except for 1 patient with impaired renal
function, all received a short course of cyclosporine, starting with
3 mg/kg per day intravenously by continuous infusion the day before
BM infusion, and continued for 28 days. Cyclosporine dose was

Reduced renal function decreased, regardless of cyclosporine serum
levels. Thereafter, cyclosporine was administered orally every 12
hours in a dose that gave serum trough levels comparable with the
intravenous infusion but was reduced (or stopped) if serum creatinine
level increased, hypertension developed, or gastrointestinal toxicity
(nausea and/or emesis) occurred. In principal, cyclosporine dose was
tapered 3 months after and discontinued in the fourth month after BMT.
Patients received filtered (leukocyte-poor) red blood cell transfu-
sions and filtered platelet concentrates from random donors. Ini-
tially, platelet concentrates from cytomegalovirus (CMV)-negative
donors were administered if patients were CMV-negative.27 All
blood products were irradiated (3,000 cGy).

Engraftment of the donor BM was documented by BM examination
and by increasing peripheral blood cell counts. When possible,
the presence of donor cells was shown by cytogenetic studies
(sex-mismatch or different fluorescent polymorphisms). Since 1989,
analysis of donor cells was performed by DNA restriction fragment-
length polymorphism (RFLP) or by amplification of the tandem-
repetitive sequences of hypervariable regions of human DNA
(VNTR).

BM aspirates/biopsies and cytogenetic studies were routinely per-
formed 100 days after BMT and repeated at 1 and 2 years posttrans-
plant. RFLP/VNTR studies were performed 6, 12, and 24 months
posttransplant. Moreover, BM, cytogenetic and DNA studies were
repeated if clinically indicated.

The diagnosis and grading of acute and chronic GVHD was estab-
lished according to the Seattle criteria.2 Chronic GVHD was defined
if GVHD was present ongoing day 90. Skin biopsies were taken
from all patients with skin rashes. If diarrhea or liver function abnor-
malities occurred after engraftment was established, biopsy speci-
mens were taken from intestinal mucosa or liver. Acute GVHD
grade I was treated with topical corticosteroids; acute GVHD grade
II was usually treated with systemic corticosteroids (1 mg/kg, twice
a day for 10 days, then tapered and stopped, if possible, within 3
weeks). Chronic GVHD was treated with systemic corticosteroids,
sometimes combined with azathioprine28 or cyclosporine.29 Since
June 1989, patients with latent CMV infection (CMV-positive)
received ganciclovir (2.5 or 5.0 mg/kg IV twice a day for 14 days),
if the CMV infection reactivated or if they were treated with high-
dose corticosteroids during the first 4 months after BMT.

Treatment of the donor BM. T-cell depletion was performed using
soybean agglutinin (SBA) and rosetting with 2-aminoethyl-
isothiouraninium bromide (AET)-treated sheep red blood cells (E).
First, BM mononuclear cells were isolated from the BM suspension
after filtration, centrifugation, and another centrifugation over Ficoll-
Isopaque. From the mononuclear cell fraction, 1% to 2% was set
apart, and the number of T cells was counted by E-rosette-forming
cells per 3,000 cells scored (in duplicate). Second, from the bulk
(98% to 99%) BM mononuclear cells the T cells were depleted by

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<th>Table 1. Patient Characteristics</th>
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<td>Characteristics</td>
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<td>No. &gt;40 yr</td>
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<td>SAA</td>
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<td>Donor to recipient sex-match</td>
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<td>Female to male</td>
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<td>Female to female</td>
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| Abbreviations: MDS, myelodysplastic syndrome; SAA, severe aplastic anemia. |

<table>
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<tr>
<th>Table 2. Patients With Standard-Risk Leukemias</th>
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<td>No. of patients studied</td>
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<tr>
<td>Age (yr), median (range)</td>
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<tr>
<td>Male/Female</td>
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<tr>
<td>No. of patients with AML</td>
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<tr>
<td>Median months from remission to BMT (range)</td>
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<tr>
<td>No. of patients with ALL</td>
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<td>Median months from remission to BMT (range)</td>
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<tr>
<td>No. of patients with CML</td>
</tr>
<tr>
<td>Median months from diagnosis to BMT (range)</td>
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Standard-risk leukemias are defined as follows: patients with AML in first remission, patients with ALL in first or second remission, and patients with CML in first chronic phase.
agglutination with SBA and differential sedimentation over bovine serum albumin (5%) gradient, followed by incubation with E in the unagglutinated (SBA−) cells, and depleted of E-rosette-forming cells by centrifugation over Ficoll-Isoopaque. In T-cell depleted BM graft the number of residual T cells was counted by E-rosette-forming cells per 3,000 cells scored (in duplicate). Third, the shortage of T cells in the (bulk) BM graft was adjusted by the addition of T cells from the small (unmodified) BM fraction to obtain $1 \times 10^5$ T cells/kg. The treated BM graft was infused immediately after cell processing through a central venous access.

Statistical methods. The probabilities of survival, relapse, relapse-free survival, and freedom from acute and chronic GVHD were estimated from the day of transplant (day 0) by the method of Kaplan and Meier.

RESULTS

BM graft. The cellular composition of the BM allograft before and after in vitro treatment is shown in Table 3. After in vitro treatment, 3% of the harvested nucleated cells was left over, containing 39% and 29% of the harvested number of colony-forming units-granulocyte macrophage (CFU-GM) and burst-forming units-erythroid (BFU-E), respectively. The number of T cells was markedly reduced to 0.34% of the harvested number. The harvested BM contained a median of 107.8 (range, 29.2 to 258.8) $\times 10^5$ T cells/kg body weight, and in vitro treatment resulted in a median of 0.39 (range, 0.00 to 1.60) $\times 10^5$ T cells/kg. Except for 1 (high-risk) patient whose BM graft contained 1.60 $\times 10^5$ T cells/kg after maximal T-cell depletion, in vitro treatment always resulted in less than $1 \times 10^5$ T cells/kg. The acquisition of $1 \times 10^5$ T cells/kg in the BM graft required the addition of a median of 46 (range, 9 to 119) $\times 10^5$ T cells/kg from the unmodified BM to the maximal T-cell depleted BM graft in the remaining 69 patients.

Graft function. Engraftment was achieved in all patients and no graft rejections were observed. The rate of engraftment, measured as recovery of granulocyte counts above 500 cells/$\mu$L, occurred after a median of 20 days (range, 12 to 44 days) posttransplantation, and the recovery of platelet counts above 50,000 cells/$\mu$L (without platelet support) occurred after a median of 28 days (range, 15 to 291 days); 3 patients could not be evaluated for the recovery of platelets above 50,000 because of early death.

Analysis of chimerisms by cytogenetic studies of BM preparations and of phytohemagglutinin-stimulated peripheral blood cells, performed in sex-mismatched BMT (or with different polymorphisms) 12 and 24 months after transplantation, and, recently, also by DNA analysis (RFLP and VNTR) of peripheral blood cells exclusively showed donor cells in patients studied in remission.

Table 3. Cell Recoveries Before and After In Vitro Treatment of the BM

<table>
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<th>Harvested BM Median (range)</th>
<th>After In Vitro Treatment Median (range)/%</th>
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<tbody>
<tr>
<td>Nucleated cells ($\times 10^5$/kg)</td>
<td>2.7 (1.5-4.4)</td>
<td>0.07 (0.02-0.17)/3</td>
</tr>
<tr>
<td>CFU-GM ($\times 10^5$/kg)</td>
<td>5.7 (0.4-18.3)</td>
<td>2.1 (0.2-13.0)/59</td>
</tr>
<tr>
<td>BFU-E ($\times 10^5$/kg)</td>
<td>4.1 (0.3-21.4)</td>
<td>1.2 (0.2-8.1)/29</td>
</tr>
<tr>
<td>T cells ($\times 10^5$/kg)</td>
<td>107.8 (29.2-258.8)</td>
<td>0.37 (0.00-1.60)/0.34</td>
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</table>

GVHD. Of 70 patients, 49 (70%) developed acute GVHD at a median of 17 days (range, 11 to 58 days) after transplant; 23 patients had grade I, and 26 patients had grade II acute GVHD. In all 49 patients, acute GVHD was limited to the skin, and no patient had organ involvement. Two patients had bilirubin values greater than 3 mg/dL concomitant with skin rashes (grade I in both patients) but without diarrhea. Clinically, both patients had mild veno-occlusive disease of the liver. Liver biopsies were not performed because of the risk of bleeding in the early days posttransplant. The elevated bilirubin values normalized spontaneously (without corticosteroid therapy) in both patients. Figure 1 shows the cumulative incidence of grade I or grade II acute GVHD. At 60 days posttransplant, the risk for acute GVHD was 70% (95% confidence interval; 59% to 80%). No patient had grade III or grade IV acute GVHD, and 35 patients were treated for acute GVHD with systemic corticosteroids. A total of 62 patients were evaluable for development of chronic GVHD (5 patients died before day 120 without chronic GVHD, and 3 patients are still at risk). Of 62 patients, 19 (31%) developed chronic GVHD. Chronic GVHD was limited to the skin (and oral mucous membrane in 5 patients) in 18 of these 19 patients, and only 1 patient developed (de novo) gut GVHD. However, chronic GVHD was graded as extensive in 14 patients and as limited in 5 patients. Chronic GVHD progressed after preceding acute GVHD (progressive chronic GVHD) in 14 patients, developed de novo (without preceding acute GVHD) in 3 patients, and evolved after acute GVHD had disappeared on treatment (quiescent chronic GVHD) in another 2 patients. The development of chronic GVHD is shown in Fig 2. The cumulative incidence of chronic GVHD is 31% (95% confidence interval; 21% to 44%) at day 140.

Except for 1 (high-risk) patient, who died because of bacterial sepsis and in whom chronic GVHD was active and moderately responsive to immunosuppressive agents at that moment, all other patients with acute or chronic GVHD had GVHD that was responsive to treatment and became free of GVHD and of immunosuppressive drugs during follow-up. Only 8 of 40 patients alive more than 1 year after BMT
Fig 2. Probability of chronic GVHD is shown in 62 evaluable patients who received BM grafts from HLA-identical siblings.

needed low-dose immunosuppressive therapy (prednisone, 10 to 20 mg daily, in 7 patients; and azathioprine, 50 mg daily, in 1 patient) for chronic GVHD. Thus, except for 1 case, GVHD could not be considered as a primary or contributing cause of death in our study.

Relapses. Patients with standard-risk leukemias are preferable for this evaluation. Characteristics of 40 patients with standard-risk leukemias are shown in Table 2. Median follow-up of these patients is 26 months (range, 2 to 97 months). To date, 5 of 40 standard-risk patients have relapsed, 2 of 9 (22%) patients with CML and 3 of 18 (14%) patients with ALL. All 3 patients with ALL have died. However, in 2 of these 3 patients with ALL, the relapse occurred (17 and 22 months after BMT) in donor cells, as determined by cytogenetic analysis and DNA studies of the blasts in BM and peripheral blood. These relapses in donor cells have to be considered as new malignancies and not as residual diseases. Thus, 3 of 40 (8%) standard-risk patients have relapsed (Fig 3). The probability of relapse is 11% (95% CI; 4% to 31%) at 24 months. Both patients with relapsed CML (recipient cells) were treated with interferon-α and peripheral blood buffy-coat cells of their BM donors.31 achieved complete remission, and are disease-free (1 patient for already more than 2 years after this treatment). The other 6 surviving CML patients were tested with cytogenetics and with the polymerase chain reaction for residual BCR/ABL transcripts at 6 months (6 patients), at 12 months (5 patients), and at 24 months (4 patients) posttransplant. All tests were negative for residual BCR/ABL transcripts.

Twenty-six patients had high-risk diseases, and 11 (42%) relapsed. The relapse-free survival of these high-risk patients, shown in Fig 4, is 48% (95% CI; 24% to 68%) at 24 months.

Survival. Of 44 standard-risk patients, 38 (86%) are alive and well at a median follow-up of 36 months (range, 2 to 97 months). Figure 3 shows the survival of 40 patients with standard-risk leukemias. The projected survival at 5 years is 80% (95% CI; 60% to 91%) for patients with standard-risk leukemias. In contrast, only 6 of 26 (23%) high-risk patients are alive and without disease at 30 months (Fig 4).

Causes of death, complications, and quality of life. Causes of death are listed in Table 4. Of 44 standard-risk patients, 38 (86%) are alive and well at a median follow-up of 36 months (range, 2 to 97 months). Figure 3 shows the survival of 40 patients with standard-risk leukemias. The projected survival at 5 years is 80% (95% CI; 60% to 91%) for patients with standard-risk leukemias. In contrast, only 6 of 26 (23%) high-risk patients are alive and without disease at 30 months (Fig 4).

Causes of death are listed in Table 4. Of 44 standard-risk

<table>
<thead>
<tr>
<th>Causes of Death</th>
<th>Standard Risk* (n = 44)</th>
<th>High-Risk (n = 26)</th>
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<tbody>
<tr>
<td>Idiopathic interstitial pneumonia</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Aspergillus pneumonia</td>
<td>—</td>
<td>1</td>
</tr>
<tr>
<td>CMV interstitial pneumonia</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Pneumocystis carinii pneumonia</td>
<td>—</td>
<td>2</td>
</tr>
<tr>
<td>Bronchiolitis obliterans</td>
<td>—</td>
<td>1</td>
</tr>
<tr>
<td>Bacterial sepsis</td>
<td>1</td>
<td>1†</td>
</tr>
<tr>
<td>New malignancy</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Recurrent malignancy</td>
<td>1</td>
<td>11</td>
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Total no. of patients: 6

* Including 4 patients with severe aplastic anemia.
† Also had active chronic GVHD.
patients, 6 (14%) have died, 5 (11%) because of transplant-related complications (1 patient with CML, 1 patient with ALL, and 1 patient with AML, within 6 months posttransplant, because of toxicity and 2, later on, because of new malignancies) and 1 (2%) because of recurrent leukemia. On the other hand, 20 of 26 (77%) high-risk patients have died, 9 (35%) because of transplant-related complications and 11 (42%) because of recurrent disease. Chronic GVHD contributed to death in only 1 (high-risk) patient, who died from bacterial sepsis. Unfortunately, 2 patients died from Pneumocystis carinii pneumonia, probably because of poor compliance with cotrimoxazole in these patients. Since the introduction of ganciclovir prophylaxis for reactivation of latent CMV infections, no CMV pneumonias were observed. Four patients developed secondary malignancies (ALL in treated with chemotherapy and had a complete response; the nosuppressive therapy (prednisone, 10 to 20 mg daily, in 7 risk diseases, 33 were alive after BMT in 4 patients, responded completely to immuno-

sive therapy 3 months earlier and in another patient with standard-risk disease who had discontinued immunosuppres-

sive agent treatment for prophylaxis against GVHD. The standard-risk patient (with intraabdominal lymphoma) was treated with chemotherapy and had a complete response; the high-risk patient (with central nervous system lymphoma) was treated with local radiotherapy but died of lymphoma. Bronchiolitis obliterans, which developed 5 to 8 months after BMT in 4 patients, responded completely to immuno-
suppressive therapy (azathioprine, 50 to 100 mg daily) in 3 (standard-risk) patients but was the cause of death in 1 (high-

risk) patient. Quality of life was determined 1 year after BMT by the Karnofsky score. At 1 year post-BMT, 40 of 70 patients were alive, and 8 (20%) needed low-dose immu-

nosuppressive therapy (prednisone, 10 to 20 mg daily, in 7 patients; and azathioprine, 50 mg daily, in 1 patient) for chronic GVHD at that time. Of 44 patients with standard-

risk diseases, 33 were alive 1 year after BMT, and 5 of 33 (15%) needed low-dose immunosuppressive therapy (predni-

sone, 10 to 20 mg daily); however, the immunosuppressive therapy could be stopped in all patients during the second year after BMT. The Karnofsky score in these 33 patients at 1 year was ≥90% in 31 patients and 80% and 70%, respectively (the patient with secondary lymphoma), in 2 patients.

**DISCUSSION**

In this report, we show that our approach of T-cell deple-

tion in HLA-identical BMT using a fixed low number of $1 \times 10^6$ T cells/kg in the BM graft is very effective in the prevention of severe acute and chronic GVHD. This approach is certainly not concessive to function of the graft, because engraftment occurs in all recipients and none of the patients had late graft failure. Furthermore, at least in patients with standard-risk leukemias, the relapse rate is comparable with that seen in non—T-cell—depleted BM grafting.

Our approach, administering to BM recipients a fixed low number of $1 \times 10^3$ donor T cells/kg of the recipient’s body-

weight in the graft, is based on data that T-cell depletion by a two-step soybean lectin agglutination and sheep red blood cell rosette procedure resulted in 2.5- to 3-log depletion of T cells (Table 3) and that a 2-log depletion, corresponding to $1 \times 10^5$ T cells/kg, is probably effective for abrogation of severe acute GVHD.\(^3\)\(^4\) The vast majority of the total number of donor T cells infused with the graft came from unmanipulated BM cells taken apart during BM processing to acquire $1 \times 10^5$ T cells/kg. We considered the addition of these unmanipulated T cells important for the reduction of both graft failure and relapse rate.

Of course, the development of GVHD is dependent on many variables, including genetic disparities outside the HLA system between patient and donor, age, sex match, prior transfusions, conditioning regimens, and immunity against a variety of microorganisms.\(^3\)\(^5\) Therefore, the number of T cells in the graft necessary for successful prevention of severe acute GVHD will vary among different patients, and the same probably holds true for graft function and relapse. Nevertheless, the use of a fixed low number of donor T cells/kg body-weight, at the level of effective prophylaxis for severe acute GVHD, is practical and may be helpful in unraveling the complex relations between GVHD, on the one hand, and graft function and relapse, on the other hand.

In the present study, and in sharp contrast to data of other studies using T-cell—depleted BM grafts which report graft failures of up to 15%,\(^6\)\(^7\) engraftment occurred in all patients, and none had late graft rejections. The rather high-dose TBI and short-course cyclosporine used in our approach may have contributed to these successful results.\(^8\)

Acute GVHD, grade I or II, was observed in 70% of the patients but was limited to the skin in all. The incidence but not severity of acute GVHD is similar to that observed in patients receiving unmodified BM grafts and single immunosuppressive agent treatment for prophylaxis against GVHD. Chronic GVHD was observed in 31% of the patients and, except for 1 case, was again limited to the skin in all. The incidence of chronic GVHD is below the incidence (≥50%) generally observed in unmodified BM grafting,\(^6\)\(^7\) probably because our approach prevents severe acute GVHD, the major risk for chronic GVHD.\(^9\) That none of the patients with acute GVHD had organ involvement by GVHD is a remark-

able feature of our approach. Furthermore, acute and chronic GVHD were very responsive to standard immunosuppressive therapy, which is also reflected by the low transplant-

related mortality of 11% observed in standard-risk patients. The value of our approach is validated also by the fact that older patients have an increased nsk for acute and chronic GVHD,\(^3\)\(^4\) and the majority of our patients were over the age of 30 years, and 25% of the patients were over the age of 40 years.

To date, 3 of 40 (8%) patients with standard-risk leukemias have relapsed. The projected 80% survival at 5 years for patients with standard-risk leukemias is promising. Thus, the relapse rate in patients with standard-risk leukemias is not inferior to that observed in patients receiving unmodified BM grafts and single immunosuppressive agent treatment for prophylaxis against GVHD. The addition of donor T cells to the graft may be responsible for the maintenance of the desired graft-versus-leukemia effect.\(^10\)\(^11\) For separate analysis of the relapse rate in patients with CML, ALL, and
AML, the number of patients is too limited. However, the fact that the high relapse rate after (standard) T-cell-depleted BM grafting is especially applicable to CML may hold true that the high relapse rate after (standard) T-cell-depleted BM grafting. However, the number of patients is too limited. However, the number of patients is too limited to make definite conclusions about the relapse rate in patients with standard-risk diseases. However, the success rate in graft function, prevention of severe GVHD, and quality of life are firm enough to approve this approach of partial T-cell depletion in allogeneic BMT.

ACKNOWLEDGMENT

We are indebted to the nursing staff of the Department of Hematology for their excellent nursing care, to Hans van Heugten and Harry Wernert for their expert laboratory procedures, and to Joukje van der Veide for her assistance in the preparation of the manuscript.

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Allogeneic bone marrow transplantation with a fixed low number of T cells in the marrow graft [see comments]

LF Verdonck, AW Dekker, GC de Gast, ML van Kempen, HM Lokhorst and HK Nieuwenhuis