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# Allogeneic Hematopoietic Cell Transplant for HIV Patients with Hematologic Malignancies: The BMT CTN-0903/AMC-080 Trial

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We set out to assess feasibility and safety of allogeneic hematopoietic cell transplant in 17 persons with HIV in a phase II prospective multicenter trial. The primary endpoint was 100-day nonrelapse mortality (NRM). Patients had an 8/8 HLA-matched related or at least a 7/8 HLA-matched unrelated donor. Indications for transplant were acute leukemia, myelodysplasia, and lymphoma. Conditioning was myeloablative or reduced intensity. There was no NRM at 100 days. The cumulative incidence of grades II to IV acute graft-versus-host disease (GVHD) was 41%. At 1 year, overall survival was 59%; deaths were from relapsed/progressive disease (n = 5), acute GVHD (n = 1), adult respiratory distress syndrome (n = 1), and liver failure (n = 1). In patients who achieved complete chimerism, cell-associated HIV DNA and inducible infectious virus in the blood were not detectable. Blood and Marrow Transplant Clinical Trials Network 0903/AIDS Malignancy Consortium 080 was registered at www.clinicaltrials.gov (no. NCT01410344).



## INTRODUCTION

Allogeneic hematopoietic cell transplantation (alloHCT) is a safe and curative option for many patients with hematologic malignancies. Before the advent of effective antiretroviral therapy (ART), hematologic malignancies in people with HIV infection (HIV+) were associated with dismal outcomes, with opportunistic infections a common cause of mortality [1]. With ART it became clear that HIV+ lymphoma patients could achieve clinical outcomes comparable with those of the general population using standard treatment regimens, including autologous HCT [2–7].

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AlloHCT has not been as well studied in the HIV+ population. The impact of alloHCT on reservoirs of HIV has attracted considerable attention in the HIV cure research community [8–11]. In particular, the only known HIV cure was achieved in 1 patient using alloHCT from a CCR5Δ32 homozygous donor to treat acute myelocytic leukemia.

Although retrospective data proving the feasibility of alloHCT in HIV+ patients has been reported [12–15], there have been no prospective multi-institution trials. Here we report the results of the Blood and Marrow Transplant Clinical Trials Network (BMT CTN) 0903/AIDS Malignancy Consortium (AMC) 080 study. This is a phase II clinical trial designed to prospectively evaluate the safety and effectiveness of alloHCT for patients with HIV infection and hematologic malignancy in a multicenter setting.

## METHODS

### *Study Design*

Between May 2012 and December 2015 a prospective phase II multicenter trial was conducted by the BMT CTN in collaboration with the AMC. Patients with HIV infection and hematologic malignancies or myelodysplastic syndromes (MDS) were treated with either reduced-intensity conditioning or myeloablative conditioning followed by alloHCT. Reduced-intensity or myeloablative conditioning was at the discretion of the investigator. Where feasible, an attempt was made to identify hematopoietic cell donors who were homozygotes for the CCR5Δ32 polymorphism. Graft-versus-host disease (GVHD) was treated per institutional standards.

The protocol was approved by the National Heart, Lung, and Blood Institute and local institutional review boards. All patients provided informed consent. The trial is registered at www.clinicaltrials.gov as NCT01410344.

### *Eligibility Criteria*

Patients had documented HIV infection, were a minimum of 15 years of age, and had acute myeloid leukemia or acute lymphocytic leukemia in first or second complete remission, intermediate-2 or high-risk MDS with <10% marrow blasts and no circulating myeloblasts after their most recent therapy, or Hodgkin or non-Hodgkin lymphoma beyond first complete remission with at least a partial response to last treatment. Patients had either an 8/8 matched related donor at HLA-A, -B, -C (serologic typing or higher resolution), and -DRB1 (at high resolution using DNA-based typing) or at least a 7/8 matched unrelated donor at HLA-A, -B, -C, and -DRB1 (at high resolution using DNA based typing). A 7/8 matched related donor match was permitted only if an 8/8 unrelated donor could not be identified. A secondary matching criterion was the presence of homozygosity for CCR5Δ32. AlloHCT using cord blood units or T cell depletion was not allowed. Patients with history of prior alloHCT were excluded. Patients had to meet adequate organ function. Patients were also required to have a Karnofsky/Lansky performance status ≥ 70% and could not have active central nervous system disease, HIV infection resistant to all ART, or opportunistic infection unresponsive to treatment.

### *Treatment*

Four regimens were permitted for conditioning. Reduced-intensity conditioning regimens were fludarabine/busulfan and fludarabine/melphalan. Myeloablative conditioning regimens were busulfan/fludarabine or cyclophosphamide/total body irradiation. GVHD prophylaxis regimens included tacrolimus/methotrexate, tacrolimus/sirolimus, and post-transplant cyclophosphamide with tacrolimus/mycophenolate. Patients receiving busulfan-containing preparative regimens were not eligible to receive tacrolimus/sirolimus. A committee reviewed each individual patient's HIV treatment history and ART options before initiation of the transplant conditioning regimen and advised changes to minimize potential drug interactions. It was recommended that ART, except ritonavir-containing regimens, should be continued during myeloablative conditioning.

### *Outcomes*

The primary trial endpoint was 100-day nonrelapse mortality (NRM; ie, death due to any causes other than relapse of the underlying malignancy). Secondary endpoints included 100-day disease status, percentage donor chimerism, hematologic function, infections, 6-month overall survival (OS), incidence of acute and chronic GVHD, immunologic reconstitution, and impact of alloHCT on measures of HIV persistence in blood, including peripheral blood mononuclear (PBMC)-associated HIV DNA and infectious virus from resting $CD4^+$ T cells using a quantitative virus outgrowth assay.

Patients with lymphoma underwent disease status assessments before alloHCT, at day +100, and at 1 year post-alloHCT. Lymphoma responses were assessed using the Cheson criteria for determination of complete remission and complete remission plus partial remission [16]. Patients with acute leukemia and MDS were assessed as complete remission if bone marrow myeloblasts were <5% by morphologic assessment, there were no circulating blasts, the neutrophil count was ≥1000/μL, with an absence of previous cytogenetic or molecular abnormalities identified before transplantation in the bone marrow aspirate. Relapse was diagnosed as an increase in bone marrow blasts to ≥5% by morphologic assessment not attributed to other causes (eg, bone marrow regeneration) or, if <5%, the reappearance of blasts with the same leukemia phenotype as present at diagnosis, the reappearance of blasts with aberrant phenotype by flow cytometry, the reappearance of leukemic blasts in the blood, the reappearance of cytogenetic or molecular markers of disease present before transplantation, or the development of extramedullary leukemia or leukemic cells in the cerebrospinal fluid. Disease relapse for patients with MDS was diagnosed if the above criteria for evolution into acute leukemia were satisfied, or if there was reappearance of pretransplant morphologic abnormalities detected in 2 consecutive bone marrow specimens taken at least 1 month apart, or if there was reappearance of pretransplant cytogenetic abnormalities in at least 1 metaphase on each of 2 separate consecutive examinations at least 1 month apart, regardless of the number of metaphases analyzed.

Follow-up visits occurred weekly through 8 weeks post-transplant, at 100 days, 6 months, 1 year, and 2 years. Time to neutrophil recovery was defined as the first of 3 consecutive days of ≥500 neutrophils/μL following the expected nadir. Time to platelet engraftment was defined as the date platelet count was ≥20,000/μL for the first of 3 consecutive labs with no platelet transfusions during the prior 7 days. Hematopoietic function was defined as the patient achieving an absolute neutrophil count > 1500/μL, untransfused hemoglobin > 10 g/dL, and untransfused platelets > 100,000/μL. Assessment occurred at day 100 and 6 months. Toxicities were graded using the Common Terminology Criteria for Adverse Events, version 4.0. Grade 3 and higher toxicities were collected. Microbiologically documented infections were collected by site of disease, date of onset, severity, and resolution from day 0 through 1 year post-alloHCT. Recovery of Ig levels was assessed by measuring quantitative Ig levels on days +60, +180, and +365 post-alloHCT. CD4+ T cells were assessed by flow cytometry on days +60, +180, and +365 post-alloHCT. Cell-associated HIV DNA was measured by quantitative PCR targeting a highly conserved region of integrase in PBMC samples obtained twice before transplant and at 100, 180, and 360 days as previously described [17]. The limit of detection of the assays is 3 copies of HIV DNA per million PBMCs [17]. The inducible infectious HIV reservoir within resting memory $CD4^+$ T cells was measured before alloHCT and at 1 year using a quantitative viral outgrowth assay as previously described [18–20].

Acute GVHD was graded according to the BMT CTN Manual of Procedures. The time to onset of acute grades II to IV and grades III to IV GVHD was recorded as well as the maximum grade experienced. Chronic GVHD was scored according to the BMT CTN Manual of Procedures. The time to onset of limited and extensive chronic GVHD was recorded.

Adjudication of the primary cause of death was as previously described [21]. Relapse was always considered to be the primary cause of death when it occurred.

### *Statistical Analysis*

This study was a phase II multicenter trial to assess the feasibility and safety of alloHCT in HIV-infected patients. The target sample size of 15 patients provided sufficient power for the primary endpoint to demonstrate that 100-day NRM was lower than 45%. A stopping guideline to monitor 100-day NRM using a truncated sequential probability ratio test was implemented to guard against excessive mortality during the study duration. The primary analysis consisted of estimating the 100-day NRM probability along with a 95% confidence interval (CI) using the cumulative incidence function. Neutrophil recovery, platelet recovery, relapse, acute GVHD, and chronic GVHD were described using the cumulative incidence function, treating death as a competing risk. OS was described using the Kaplan-Meier estimate. Other endpoints were described using descriptive statistics including proportion. Statistical analyses were performed with SAS software, version 9.4 (SAS Institute, Cary, NC). The cumulative incidence analyses were performed with R software (Foundation for Statistical Computing, Vienna, Austria), version 2.15.1.

## RESULTS

### *Patients*

Seventeen HIV+ patients with acute leukemia, MDS, non-Hodgkin lymphoma, or classic Hodgkin lymphoma were enrolled in the clinical trial and underwent alloHCT. Three additional patients were enrolled on trial but were not included in the analysis because 2 relapsed or progressed before receiving conditioning and 1 underwent alloHCT off

study. Median follow-up for survivors as of August 10, 2018 was 24.4 months (range, 22.1 to 27.4). All living patients completed a 2-year follow-up. There were 2 significant protocol violations. One patient began the conditioning regimen on day −10 as per institutional practice rather than day −5 as required by the protocol. Another patient received an alternative GVHD prophylaxis rather than that required by the protocol. One patient who received a matched unrelated transplant had several hundred potential matched unrelated donors in the registry, and it is likely a CCR5Δ32 homozygous donor could have been identified had time permitted, but because of clinical urgency the patient and treating physicians elected to proceed with the first matched unrelated donor rather than waiting for analysis of donor CCR5 status.

Patient characteristics are presented in Table 1. All patients received T cell–replete bone marrow grafts from HLA matched sibling (n = 4) or unrelated donors (n = 9) or single-antigen mismatched sibling (n = 3) or unrelated (n = 1) donors. The pretransplant HIV plasma RNA level was below the limit of quantification in 15 of 17 patients (88.2%). The plasma HIV RNA measurements for the 2 patients with detectable levels were 82 and 101 copies/mL, respectively. The median pretransplant $CD4^+$ T cell count was 224 $CD4^+/\mu L$ (range, 55 to 833).

### *NRM, OS, Relapse, and Causes of Death*

As of August 10, 2018, 8 patients have died, with a median follow-up of 24.4 months for survivors. The primary causes of death are shown in Table 2. For all 3 patients with NRM, death occurred more than 10 months post-transplant (Figure 1A). The 1-year NRM rate was 11.8% (95% CI, 1.8%-32.2%) and the 2-year NRM rate was 18.3% (95% CI, 4.1%-40.7%). The 6-month OS was 82.4% (95% CI, 54.7%-93.9%) and 1-year OS was 58.8% (95% CI, 32.5%-77.8%) (Figure 1B). The 2-year OS was estimated to be 52.3% (95% CI, 26.8%-72.7%).

Five patients' hematologic malignancies relapsed or progressed. These events occurred by 6 months after transplant. The 1-year rate of relapse/progression was 29.4% (95% CI, 10.2%-51.9%). At the time of transplant all 11 patients with acute leukemia and 3 of 4 lymphoma patients were in complete remission. At day 100 after alloHCT 13 patients (76.5%) were in complete remission, 4 (23.5%) had relapsed or progressive disease, and 1 had relapsed and died on day +95. The cumulative incidence of relapse/progression (with death considered as a competing risk) is shown in Figure 1C.

### *Hematologic Function after AlloHCT and Lymphocyte Counts*

All patients achieved neutrophil recovery post-transplant. The median time to neutrophil recovery was 17 days (range, 11 to 22). All but 1 patient achieved platelet recovery to 20,000/$mm^3$. The cumulative incidence of platelet recovery to 20,000/$mm^3$ at day 100 was 94.1%. The median time to platelet recovery to 20,000/$mm^3$ was 19 days. The cumulative incidence of platelet recovery to 50,000/$mm^3$ at day 100 was 88.2%. The median time to platelet recovery to 50,000/$mm^3$ was 23 days. Among the 16 patients alive at day 100, 4 (25%) achieved hematologic function. Among 13 patients alive at day 180, 4 (30.8%) achieved hematologic function. Median $CD3^+$ and $CD4^+$ T cell counts returned to baseline levels by 6 months after transplant and more than doubled by 1 year post transplant.

### *Chimerism*

Chimerism results are shown in Table 3. Among 6 patients who received myeloablative conditioning and survived to 6 months, 4 had full chimerism and 2 mixed chimerism. Among 7 patients who received reduced-intensity conditioning and survived to 6 months, 5 had full chimerism and 2 mixed chimerism.

**Table 1**
Demographic and Clinical Characteristics of Patients Undergoing AlloHCT

| Characteristics | Value |
|---|---|
| Total transplanted | 17 (100) |
| Sex | |
| Male | 17 (100) |
| Ethnicity | |
| Hispanic or Latino | 1 (6) |
| Not Hispanic or Latino | 15 (88) |
| Unknown | 1 (6) |
| Race | |
| American Indian/Alaskan Native | 1 (6) |
| Black or African American | 3 (18) |
| White | 11 (65) |
| Unknown/other | 2 (12) |
| Age, yr | |
| Median (range) | 47 (25-64) |
| Performance status | |
| 100 | 4 (24) |
| 90 | 9 (53) |
| 80 | 3 (18) |
| 70 | 1 (6) |
| Patient diagnosis | |
| Acute myeloid leukemia | 9 (53) |
| Acute lymphocytic leukemia | 2 (12) |
| MDS | 2 (12) |
| Hodgkin lymphoma | 1 (6) |
| Non-Hodgkin lymphoma | 3 (18) |
| Leukemia status | |
| First complete remission | 8 (73) |
| Second complete remission | 3 (27) |
| Lymphoma status | |
| Complete remission | 3 (75) |
| Partial remission | 1 (25) |
| HIV load | |
| Undetectable | 15 (88) |
| Detectable | 2 (12) |
| Mean copies/mL | 92 |
| Pre-transplant recipient CMV serostatus | |
| Positive | 12 (71) |
| Negative | 5 (29) (3 donors positive, 2 donors negative) |
| No. of induction chemotherapy regimens | |
| 1 | 10 (59) |
| 2 | 6 (35) |
| 3 | 1 (6) |
| No. of salvage chemotherapy regimens | |
| 0 | 10 (59) |
| 1 | 6 (35) |
| 3 | 1 (6) |
| HLA match score | |
| 7/8 | 4 (24) (3 related donor, 1 unrelated) |
| 8/8 | 13 (76) (4 related donor, 9 unrelated) |
| Baseline CD4 count, cells/μL | |
| Median | 224 |

Values are n (%) unless otherwise defined. CMV indicates cytomegalovirus.

**Table 2**
Primary Causes of Death

| Cause | No. of Cases |
|---|---|
| Relapse/progression | 5 |
| Acute GVHD | 1 |
| Adult respiratory distress syndrome | 1 |
| Liver failure | 1 |
| Total | 8 |

### *Graft-versus-Host Disease*

Acute GVHD was reported in 7 patients: 4 had grade II, 2 had grade III, and 1 had grade IV. The day 100 grades II to IV acute GVHD rate was 41.2% (95% CI, 17.8%-63.4%). The day 100 grades III to IV acute GVHD rate was 11.8% (95% CI, 1.8%-31.9%). Chronic GVHD was reported for 3 patients. All the cases were mild chronic GVHD, and 2 of the 3 patients did not experience any acute GVHD. The 1-year chronic GVHD rate was 17.6% (95% CI, 4.0%-39.2%).

### *Infections*

At least 1 infectious episode was reported in 11 patients (64.7%), and the total number of infection events was 55 (Table 4). Grade 2 infections were reported in 3 patients and grade 3 in 8 patients. Infections were bacterial in 11 patients (35 infections), viral in 5 (14 infections), fungal in 3 (3 infections), protozoal in 1 (1 infection), and other in 1 patient. Details of cytomegalovirus and fungal infection are presented in Table 4. No deaths were attributed to infection.

### *Unexpected Adverse Events*

Fourteen patients (82.3%) experienced grades 3 to 5 adverse events, with 5 grade 3, 1 grade 4, and 8 grade 5. The most commonly reported adverse events were gastrointestinal disorders, vascular disorders, chemistry/investigations, metabolism, and nutrition disorders. In addition to the grades 3 to 5 adverse events, 3 patients experienced abnormal liver function. One patient developed acute renal failure and was dialyzed.

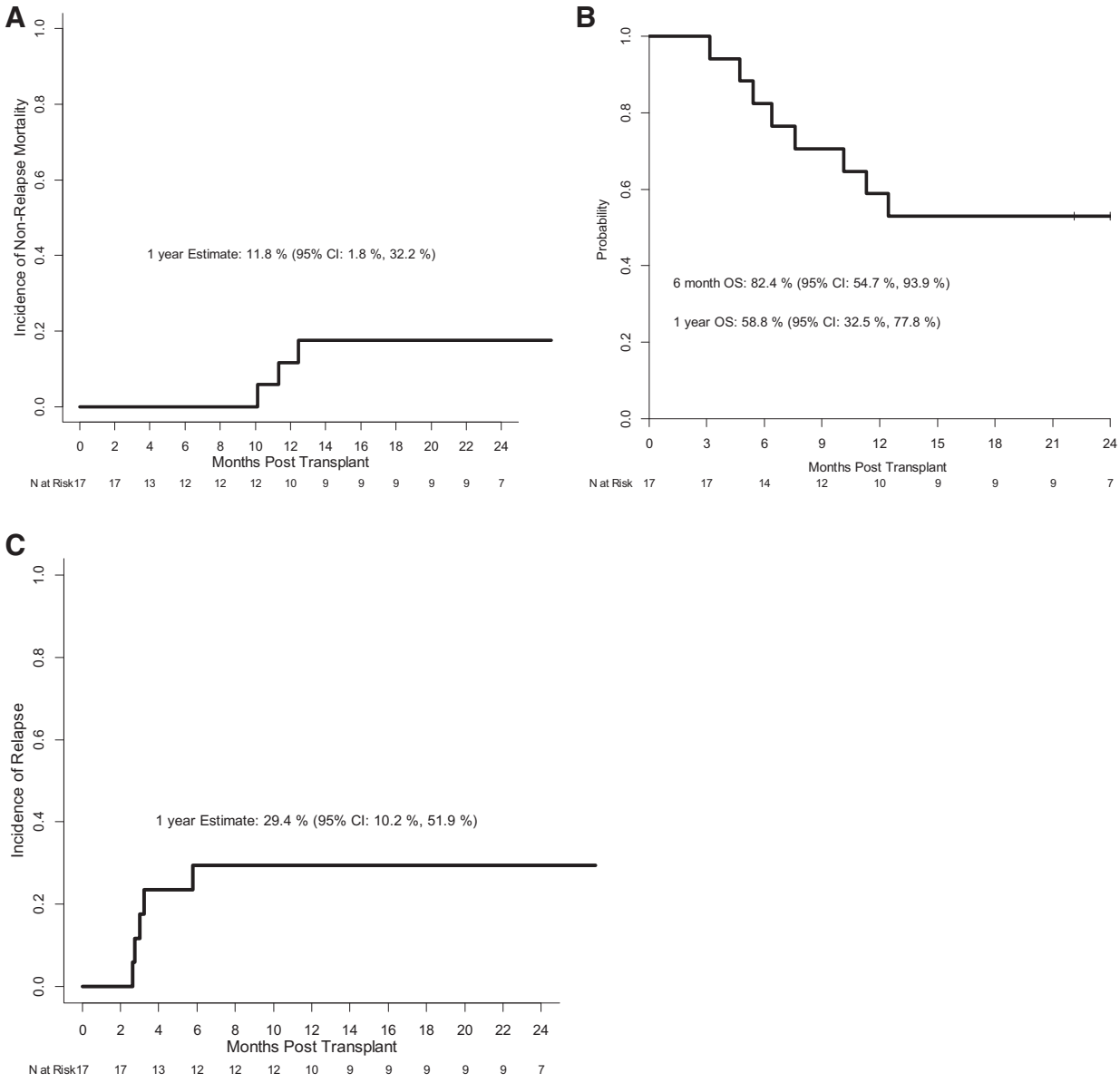


**Figure 1.** NRM, OS, and cumulative incidence of relapse/progression post-transplant. (A) NRM, (B) OS, and (C) relapse for 17 patients undergoing alloHCT.

**Table 3**
Chimerism after AlloHCT by Conditioning Regimen

| Assessment Time Point Post-Transplant | Full Chimerism | Mixed Chimerism | Graft Rejection | Total Participants Surviving/Followed to Time Point |
|---|---|---|---|---|
| Myeloablative conditioning (n = 8) | | | | |
| At 4 weeks | 4 (57) | 2 (29) | 1 (14) | 7 (100) |
| At day 100 | 3 (43) | 4 (57) | 0 (0) | 7 (100) |
| At 6 months | 4 (67) | 2 (33) | 0 (0) | 6 (100) |
| Reduced-intensity conditioning (n = 9) | | | | |
| At 4 weeks | 5 (56) | 4 (44) | 0 (0) | 9 (100) |
| At day 100 | 5 (56) | 4 (44) | 0 (0) | 9 (100) |
| At 6 months | 5 (71) | 2 (29) | 0 (0) | 7 (100) |

Values are n (%). Donor chimerism based on T cell assays: full (>95% donor cells), mixed (5-95%), or graft rejection (<5%). If T cell assay was not done, bone marrow samples were used. If bone marrow assay was not done, blood samples were used.
*One patient did not have chimerism assessed on day 28.

### *Changes in Markers of HIV Persistence in Blood*

This trial allowed for a search to identify potential CCR5Δ32 homozygous donors. Only 1 patient had a suitable CCRΔ32 donor identified. This patient experienced leukemic relapse, thus precluding any long-term assessment of the impact of alloHCT on HIV reservoirs.

The number of HIV infected cells in the blood was assessed by quantitative PCR targeting the integrase region of proviral DNA in PBMCs (Figure 2). Analysis of time points where chimerism was measured in parallel with cell-associated HIV DNA showed that at every time point in 8 patients who were complete chimeras, cell-associated HIV DNA was undetectable. In contrast, in 9 measurements in 6 patients who were mixed chimeras, cell-associated HIV DNA was detected at a median of 85 copies per million (range, 0 to 174). A quantitative viral outgrowth assay was performed in patients who survived to 1 year (n = 8), had undetectable plasma HIV by standard clinical assay (n = 6), and agreed to a large-volume blood draw (n = 5). Among 3 patients who had achieved complete donor T cell chimerism, inducible infectious virus was not detected post-transplant. In 1 of these patients viral outgrowth assay had also been negative for infectious virus pretransplant. Among 2 patients who demonstrated mixed chimerism at 1 year, infectious HIV remained detectable in resting $CD4^+$ T cells by the quantitative viral outgrowth assay in both.

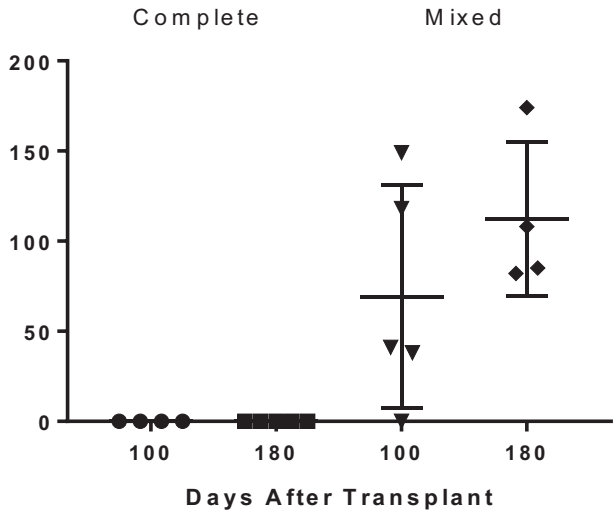


**Figure 2.** Dot plot showing cell-associated HIV DNA per million PBMCs in patient with complete chimerism or mixed chimerism at 100 or 180 days after transplant. Means, standard deviations, and individual data points are shown.

## DISCUSSION

We undertook a prospective multi-institutional trial of alloHCT in HIV+ patients with a primary endpoint of 100-day NRM. There was no NRM at 100 days or at 6 months and therefore no evidence to suggest that NRM is prohibitive or in excess of that seen in non–HIV-infected patients. Our findings demonstrate the safety and feasibility of alloHCT for HIV+ patients who meet standard transplant criteria and who have treatment-responsive HIV infection. Our findings are consistent with a recent retrospective review of HIV patients who underwent autologous or alloHCT [15]. That analysis, which included a similar number of alloHCT patients to ours, compared patients in the database with HIV with matched patients without HIV and found no difference in inpatient mortality rates.

**Table 4**
Infections

| Grade | Site of Infection | Date of Onset (Post-Transplant) (day) | Organism | Treatment | Survival Status (Primary Cause of Death) |
|---|---|---|---|---|---|
| Grade 2 | Blood | 39 | CMV | Ganciclovir | Died on day 308 (adult respiratory distress syndrome) |
| Grade 2 | Blood | 119 | CMV | Foscarnet | Died on day 194 (relapse) |
| Grade 2 | Blood | 124, 260 | CMV | Ganciclovir, valacyclovir | Died on day 379 (acute GVHD) |
| Grade 2 | Blood | 36 | CMV | Valganciclovir | Died on day 143 (relapse) |
| Grade 2 | Tongue, oral cavity, and oropharynx | 248 | Candida | Nystatin | Died on 344 (liver failure) |
| Grade 2 | Upper airway and nasopharynx | 211 | Pneumocystis | Trimethoprim/sulfamethoxazole | Alive at day 751 |
| Grade 3 | Feces/stool | 35 | *Candida krusei* | Voriconazole | Alive at day 741 |

The present study was too small to allow a comparative analysis of preparative or GVHD prophylaxis regimens [22,23]. However, we note that T cell depletion, cord blood, and haploidentical donor strategies were not evaluated in this trial.

As in the general population undergoing alloHCT, relapse of malignancy remains the main cause of treatment failure. There is no evidence from this trial to suggest any increased risk of disease relapse in the HIV+ population. The lack of additional relapses after 6 months post-HCT, however, is encouraging.

A little over half of the patients (56%) achieved complete donor chimerism at 4 weeks, which increased at 6 months (69%). There is no single benchmark for assessing complete chimerism rates after alloHCT. Chimerism is related to both disease type and preparative regimen. It should be noted that neither antithymocyte globulin nor T cell depletion was used in any of these transplants. The limitations of the study (small sample size, heterogeneous indications for transplant, varying preparative regimens) precluded any conclusions as to whether disparities in chimerism rates exist in HIV+ patients compared with non–HIV-infected patients, but the question is important because mixed chimerism inevitably leads to HIV persistence.

There have now been 2 reports of virologic cure of HIV infection using CCR5Δ32 homozygous donors [9,24]. Another HIV patient with peripheral T cell lymphoma who received myeloablative alloHCT from a CCR5Δ32 homozygous donor had rapid HIV rebound after transplant with a highly replicative CXCR4-tropic HIV variant [25]. As noted above, the only patient in this series to receive an alloHCT from a CCR5Δ32 homozygous donor relapsed with acute myeloid leukemia early post-transplant and thus was unable to provide confirmatory evidence that alloHCT can potentially cure HIV infection. However, in patients who received CCR5 wild-type donors in this series and achieved complete donor chimerism, HIV-1 was not detected in PBMCs using a sensitive quantitative PCR assay for proviral DNA [17] and infectious virus was not detected using a quantitative viral outgrowth assay. This is consistent with earlier reports that when complete T cell donor chimerism is achieved, the number of HIV-infected cells in blood is reduced to levels below the limits of detection of these assays [10,26,27]. These reductions in HIV-infected blood cells in peripheral blood do not mean that all infected cells including those with intact (replication-competent) proviruses were eliminated. Indeed, evidence from prior alloHCT patients suggests that despite undetectable HIV DNA in blood, interruption or cessation of ART can be associated with aggressive viral rebound, illustrating that blood measures are not adequate to detect all latent HIV in allograft recipients [10,28,29]. In studies focused on HIV cure rather than treatment of hematologic malignancy, comprehensive analyses of memory T cells within gastrointestinal lymphoid tissue and lymph nodes have been undertaken, but such studies were not performed here. The present study is also limited by the small number of patients assessed. Nonetheless, at present, alloHCT is the only intervention shown to reduce markers of HIV persistence in blood to undetectable levels. Whether this reduction has biologic importance with regard to the course of HIV infection or the potential to achieve ART-free HIV remission is not known.

We note that 1 patient who received a matched unrelated donor transplant and had hundreds of potential HLA matched unrelated donors decided not to wait for further donor screening to identify a CCR5Δ32 homozygous donor. Since the time of this trial, many registries have begun screening donors routinely, and HIV-resistant donors can sometimes be identified very rapidly.

Very recently similar data have been published from an international collaboration to investigate HIV cure by stem cell transplantation [30]. Among 23 HIV patients undergoing allogeneic transplants, 13 died within 2 years. Among patients who achieved complete donor chimerism, there was a profound long-term reduction in the HIV reservoir. The analyses reported included investigation of HIV in lymph nodes, bone marrow, and cerebrospinal fluid in some cases.

In addition to validating the safety of alloHCT in HIV+ patients, this trial also demonstrates the reconstitution of Ig levels and $CD4^+$ T cell counts post-transplant. Thus, we saw no evidence to suggest that alloHCT was associated with a long-term deterioration in cellular immunity. Similarly, IgG levels recovered by 1 year post-transplant.

The BMT CTN 0903/AMC 080 trial represents the only prospective multi-institutional study of the use of alloHCT in HIV+ patients. The safety outcomes in this trial coupled with previously published alloHCT data indicated that HIV infection should not be considered a contraindication to alloHCT in patients who otherwise meet standard transplant inclusion criteria and in whom HIV plasma RNA can be suppressed with ART. Patients with HIV infection should also be considered appropriate for participation in clinical trials aimed at reducing relapse or progression of malignant disease and other approaches to improve overall outcomes.

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