

CORRESPONDENCE



HIV-1 Remission after Allogeneic Hematopoietic-Cell Transplantation

TO THE EDITOR: We report the results of the 60-month follow-up of a 63-year-old man who was found to be free of human immunodeficiency virus type 1 (HIV-1) infection after undergoing hematopoietic-cell transplantation (HCT) for the treatment of acute myelogenous leukemia (AML). The transplant was obtained from a donor with a $\Delta 32$ mutation, which causes a *CCR5* deletion (*CCR5- $\Delta 32/\Delta 32$*) that has been associated with resistance to HIV-1 infection. At the time of this follow-up, the patient had been free of HIV-1 infection for 35 months after the discontinuation of antiretroviral therapy. The patient had received a diagnosis of HIV-1 infection 31 years before undergoing transplantation, and because of his older age, he had received reduced-intensity conditioning without T-cell depletion, unlike other HCT recipients who have had prolonged HIV-1 control (Table S1 in the Supplementary Appendix, available with the full text of this letter at NEJM.org).¹⁻⁴

The patient, who had a history of undetectable HIV-1 RNA levels since 1997 while receiving antiretroviral therapy, had remission from AML after salvage chemotherapy (Table S2). HCT was recommended for AML cure, and a *CCR5- $\Delta 32/\Delta 32$* donor was identified. The patient had wild-type homozygous *CCR5* receptors and predominantly R5 virus. After approval by the institutional review board at City of Hope National Medical Center, the patient consented to reservoir testing and eventual interruption of his antiretroviral therapy to assess HIV remission.

HCT was performed with the use of reduced-intensity conditioning with fludarabine and melphalan as well as sirolimus–tacrolimus prophylaxis against graft-versus-host disease (GVHD) (Fig. 1A). The patient and donor were matched with respect to human leukocyte antigen (Table S3A) with different genotypes of killer-cell im-

munoglobulin-like receptors (KIRs) (Table S3B). After HCT, bone marrow biopsy was negative for AML with full donor-cell chimerism. Immunity to hepatitis B virus was noted after vaccination.

HIV-1 RNA levels were undetectable both before and after HCT. HIV DNA was detected in peripheral blood mononuclear cells (PBMCs) before HCT and was mostly undetectable afterward in both PBMCs (Fig. 1B) and in gut tissue (Fig. 1C and Table S4).¹⁻⁴ Interruption of antiretroviral treatment was initiated 25 months after HCT, according to published recommendations.⁵ Since that time, HIV-1 RNA and cellular DNA and RNA have been undetectable, and CD4 counts have ranged from 356 to 1271 cells per microliter (Table S5).

After HCT, testing for intact proviral DNA revealed a more than 2-log reduction in total proviruses, with no intact and total proviruses detected after treatment interruption (Table S6). Six months after treatment interruption, the patient's cells were resistant to *in vitro* infection by HIV-1 *CCR5* strains but not by *CXCR4* or dual-tropic virus strains. In contrast, detectable p24 antigen levels developed in CD8-depleted PBMC samples obtained from two healthy controls (Fig. 1D). A total of 12 months after treatment interruption, the patient's T cells showed activation in response to CD3/CD28 beads and cytomegalovirus (CMV) peptide mix, whereas no responses were observed

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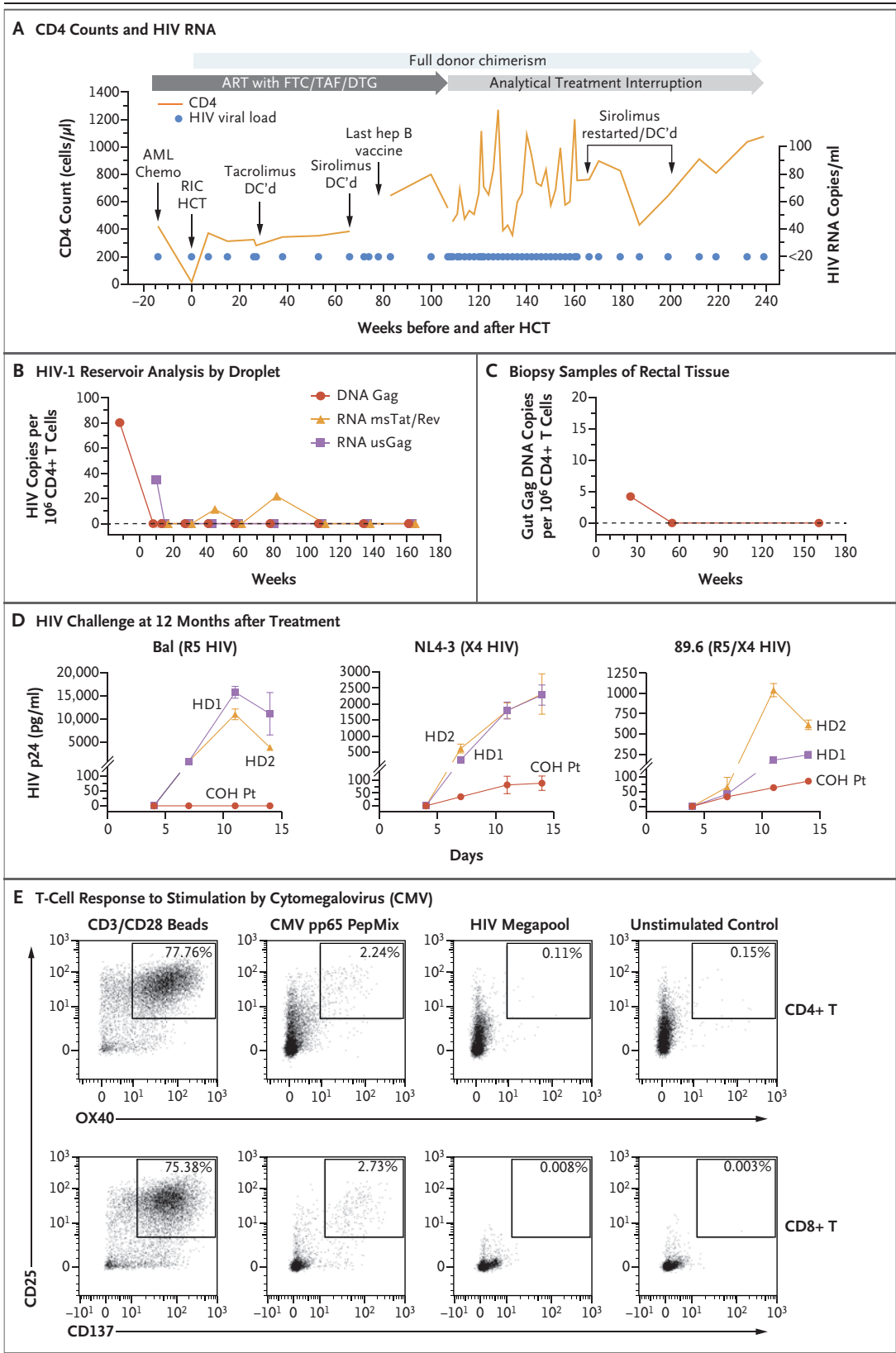


Figure 1 (facing page). Patient's Course of Treatment and Immunologic Studies.

Panel A shows the patient's CD4 counts (orange line) and HIV RNA (blue dots) over time relative to treatment with induction chemotherapy, the course of hematopoietic-cell transplantation (HCT) for the treatment of acute myelogenous leukemia (AML), and interruption of antiretroviral treatment (ART). Also shown is HIV-1 reservoir analysis by droplet digital polymerase chain reaction on the patient's cellular DNA and RNA at indicated time points in samples of peripheral blood mononuclear cells (PBMCs) (Panel B) and biopsy samples of rectal tissue (Panel C). Data show the number of copies per 1 million CD4 T cells. Panel D shows the HIV challenge at 12 months after treatment interruption. CD8-depleted PMBCs were challenged with HIV BaL (R5), NL4-3 (X4), and 89.6 (R5X4) strains, and levels of HIV p24 were measured by enzyme-linked immunosorbent assay in culture supernatants in duplicate. Panel E shows T-cell responses to stimulation by cytomegalovirus (CMV) and HIV peptide pools with the use of activation-induced marker (AIM) flow assay at 12 months after treatment interruption. PBMC samples were cultured with the respective peptide pools for 20 hours; viral responsive CD4 T cells were defined according to CD25 and OX-40 expression, and CD8 T cells were defined according to CD25 and CD137 expression. COH Pt denotes City of Hope study patient, DC'd discontinued, DTG dolutegravir, FTC emtricitabine, Gag group-specific antigen, HD healthy donor, RIC reduced-intensity conditioning, RNA msTat/Rev multiply spliced RNA encoding for transactivation of transcription (Tat) and regulator of expression of virion proteins (Rev), TAF tenofovir alafenamide, and usGag unspliced RNA encoding Gag.

with HIV peptide mix, which indicated the patient's T-cell exposure to CMV but not to HIV (Fig. 1E).

At the time of this report, the patient remains in remission from HIV and AML while receiving topical treatment for oral GVHD. His blood, bone marrow, and reservoir sites converted to full chi-

merism with CCR5-Δ32/Δ32 donor cells. This case has shown that older patients who are undergoing reduced-intensity conditioning HCT for the treatment of cancer may be cured of HIV-1 infection.

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Decolonization in Nursing Homes to Prevent Infection

TO THE EDITOR: The Protect trial by Miller et al. (Nov. 9 issue)¹ included patients admitted with infectious diseases according to diagnosis codes as listed in the *International Classification of Diseases, 10th Revision (ICD-10)*. Detailed classification of infections, according to organ of infection, and definitive culture results of these hospitalized patients

were unavailable, and it is unclear whether the effect of the intervention was due to reduced infections caused by multidrug-resistant organisms (MRDOs), as investigated in the sampling. For example, chlorhexidine baths have been reported to be beneficial in reducing infections, such as central venous catheter-associated bloodstream and